MPsrch_pp protein - protein database search, using Smith-Waterman algorithm

Run on: Fri Sep 15 16:31:53 2000; MasPar time 7.33 Seconds
659.137 Million cell updates/sec

Tabular output not generated.

Title: >US-09-230-048-2
Description: (1-204) from US09230048.pep
Perfect Score: 1579
Sequence: 1 MCWFKLWSLLLVGSLLVSGT.....GQAVRVLDSIPDVTPDVHDK 204

Scoring table: PAM 150
Gap 11

Searched: 188963 seqs, 23686106 residues

Post-processing: Minimum Match 0%
Listing first 45 summaries

Database: a-geneseq36
1:geneseqp

Statistics: Mean 33.281; Variance 144.471; scale 0.230

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description	Pred. No.
1	1579	100.0	204	1	W74570	Kaposi sarcoma herpes-	9.31e-140
2	1579	100.0	204	1	W40103	Human herpesvirus 8 (H	9.31e-140
3	1579	100.0	204	1	W23944	Human herpesvirus 8 in	9.31e-140
4	1413	89.5	185	1	W95015	Kaposi's sarcoma herpe	1.80e-123
5	265	16.8	184	1	W02611	Interleukin-6 (F74Y, Q	2.01e-13
6	264	16.7	184	1	W92803	Human IL-16 mutein pro	2.47e-13
7	264	16.7	184	1	W07200	Human interleukin 6 an	2.47e-13
8	264	16.7	184	1	W08477	Interleukin-6 variant	2.47e-13
9	264	16.7	184	1	W58519	Human interleukin 6 mu	2.47e-13
10	263	16.7	184	1	W02610	Interleukin-6 (Q75Y, S	3.04e-13
11	262	16.6	184	1	W08476	Interleukin-6 variant	3.73e-13
12	258	16.3	185	1	R45720	Full length interleuki	8.48e-13
13	257	16.3	185	1	R45718	Full length interleuki	1.04e-12
14	256	16.2	212	1	W33643	Human interleukin-6 (I	1.28e-12
15	256	16.2	212	1	W35878	Human interleukin-6 (I	1.28e-12
16	252	16.0	169	1	R77387	Human IL-6 mutant IL-6	2.89e-12
17	253	16.0	184	1	W02612	Interleukin-6 (Q75Y, S	2.36e-12
18	253	16.0	184	1	W07197	Human interleukin 6 an	2.36e-12
19	253	16.0	184	1	W07198	Human interleukin 6 an	2.36e-12
20	252	16.0	184	1	R54990	Mutant Interleukin 6 S	2.89e-12
21	252	16.0	184	1	W08478	Interleukin-6 variant	2.89e-12
22	252	16.0	184	1	R03914	Polypeptide with human	2.89e-12
23	252	16.0	184	1	R20783	Interleukin-6.	2.89e-12
24	252	16.0	184	1	W58518	Human interleukin 6 mu	2.89e-12
25	252	16.0	184	1	R68623	B-cell differentiation	2.89e-12
26	252	16.0	184	1	R06532	Human B-cell simulator	2.89e-12
27	252	16.0	184	1	W02609	Interleukin-6.	2.89e-12
28	253	16.0	185	1	R05311	Segment of B-cell diff	2.36e-12
29	253	16.0	185	1	R45719	Full length interleuki	2.36e-12
30	252	16.0	185	1	R68624	Ala-BCDF.	2.89e-12
31	252	16.0	185	1	P91015	Synthetic interleukin-	2.89e-12
32	252	16.0	185	1	R05275	Segment of human B cel	2.89e-12
33	252	16.0	185	1	R45717	Full length interleuki	2.89e-12
34	252	16.0	187	1	R13471	hIL-6 protein.	2.89e-12
35	252	16.0	188	1	W95011	Human interleukin-6 (I	2.89e-12
36	252	16.0	212	1	R49249	Sequence of human B-ce	2.89e-12
37	252	16.0	212	1	R34726	Human IL-6 (for modifi	2.89e-12
38	252	16.0	212	1	P90047	pBSF2-L8 sequence	2.89e-12
39	252	16.0	212	1	R33430	IFN-beta-2a.	2.89e-12
40	252	16.0	212	1	P90371	pBSF2-L8	2.89e-12
41	252	16.0	212	1	R72317	Interferon-beta2A.	2.89e-12
42	252	16.0	212	1	P81156	Human B-cell different	2.89e-12
43	252	16.0	212	1	P90469	Interleukin-6	2.89e-12
44	252	16.0	525	1	W36846	Human fusion polypepti	2.89e-12
45	252	16.0	543	1	Y03164	Chimeric sIL-6R/IL-6 p	2.89e-12

ALIGNMENTS

RESULT 1
ID W74570 standard; Protein; 204 AA.
AC W74570;
DT 04-DEC-1998 (first entry)
DE Kaposi sarcoma herpes-like virus/interleukin-6.
KW Kaposi sarcoma herpes-like virus/interleukin-6; PCR; primer;
KW antiviral agent; multiple myeloma; vaccine; rheumatoid arthritis;
KW monoclonal gammopathy of undetermined significance; MGUS; malignant;
KW interleukin-6; Alzheimer's disease; multiple sclerosis; scleroderma;
KW systemic lupus erythematosus; amplification.
OS Synthetic.
PN WO9835684-A2.
PD 20-AUG-1998.
PF 12-FEB-1998; U02820.
PR 11-NOV-1997; US-967504.
PR 14-FEB-1997; US-800710.
PA (BERE/) BERENSON J R.
PA (RETT/) RETTIG M B.
PA (VESC/) VESCIO R A.
PI Berenson JR, Rettig MB, Vescio RA;
DR WPI; 98-480765/41.
DR N-PSDB; V54070.
PT Treatment of multiple myeloma and monoclonal myopathy with antiviral
PT agent - active against Kaposi sarcoma virus, or with inhibitory
PT nucleic acid or antibody against this virus
PS Disclosure; Fig 5B; 137pp; English.
CC This is the amino acid sequence of the kaposi sarcoma herpes-like
CC virus/interleukin-6, used in the method of the invention. In this
CC method, an antiviral agent effective against Kaposi sarcoma
CC herpes-like virus (KSHV), is used to prevent progression of MGUS to
CC multiple myeloma or related malignancy. KHSV- and/or interleukin-6
CC related disorders such as specifically Alzheimer's disease, multiple
CC sclerosis, rheumatoid arthritis, systemic lupus erythematosus,
CC scleroderma and malignancies of kidney or head/neck. The vaccines
CC (comprising a KHSV-specific immunogen) is used to produce a
CC therapeutic and/or prophylactic response.
SQ Sequence 204 AA;

Query Match 100.0%; Score 1579; DB 1; Length 204;
Best Local Similarity 100.0%; Pred. No. 9.31e-140;
Matches 204; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Db      1 MCWFKLWSLLLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy      1 MCWFKLWSLLLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60

Db     61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120
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                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy      61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120

Db     121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy     121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180

Db     181 EKFAGQAVRVLDSIPDVTPDVHDK 204
           |||||||||||||||||||||||||
Qy     181 EKFAGQAVRVLDSIPDVTPDVHDK 204


RESULT    2
ID   W40103 standard; Protein; 204 AA.
AC   W40103;
DT   15-JUL-1998  (first entry)
DE   Human herpesvirus 8 (HHV-8) interleukin-6.
KW   DL-B; thymidylate synthase; dihydrofolate reductase; primer; HHV-8;
KW   Bcl-2 homologue; IE-1A; IE-1B; viral macrophage inhibitory protein;
KW   Kaposi's sarcoma; beta-chemokine-like; amplification; PCR; vIL-6.
OS   Kaposi's sarcoma associated herpesvirus.
PN   WO9804284-A1.
PD   05-FEB-1998.
PF   24-JUL-1997; U12931.
PR   25-JUL-1996; US-022591.
PA   (UYJO ) UNIV JOHNS HOPKINS.
PI   Hardwick JM, Hayward GS, Nicholas J, Reitz MR;
DR   WPI; 98-130422/12.
PT   New human herpes virus gene region containing 8 open reading frames
PT   - useful for, e.g. diagnosing Kaposi's sarcoma or body cavity based
PT   large cell lymphoma
PS   Claim 1; Pages 59-60; 84pp; English.
CC   The sequence represents a novel human herpesvirus 8 (HHV-8)
CC   interleukin-6.  The invention claims for novel genes, which includes
CC   the viral interleukin-6 gene, found at the divergent DL-B locus.  HHV-8
CC   divergent locus DL-B lies between open reading frames 11 and 17.
CC   Sequencing of the HHV-8 divergent locus DL-B revealed the presence of
CC   nine viral ORFs with gene products related to cellular proteins.  These
CC   proteins include the thymidylate synthase (TS, W40100), dihydrofolate
CC   reductase (DHFR, see W40101), Bcl-2 homologue (W40102), IE-1A (W40107),
CC   IE-1B (W40108) and, four cytokines which include viral interleukin-6
CC   (vIL-6), viral macrophage inhibitory protein (vMIP)-1A (W40104) and -1B
CC   (W40105) and beta-chemokine-like (BCK, W40106) protein.  The invention
CC   claims the mentioned proteins and a polynucleotide containing HHV-8
CC   genes encoding one or more of these proteins.  The invention also claims
CC   that the polynucleotide and the proteins may be used directly or
CC   indirectly, e.g. using antibodies to the proteins, to diagnose an HHV-8
CC   associated disease, e.g. Kaposi's sarcoma, Castleman's disease, multiple
CC   myeloma and body cavity based large cell lymphoma (BCBL).  The proteins
CC   have also been claimed to be useful in screening compounds for drugs to
CC   treat HHV-8 diseases.
SQ   Sequence   204 AA;

  Query Match          100.0%;  Score 1579;  DB 1;  Length 204;
  Best Local Similarity 100.0%;  Pred. No. 9.31e-140;
  Matches   204;  Conservative    0;  Mismatches   0;  Indels   0;  Gaps   0;

Db       1 MCWFKLWSLLLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy       1 MCWFKLWSLLLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60

Db      61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy      61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120

Db     121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy     121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180

Db     181 EKFAGQAVRVLDSIPDVTPDVHDK 204
           |||||||||||||||||||||||||
Qy     181 EKFAGQAVRVLDSIPDVTPDVHDK 204


RESULT    3
ID   W23944 standard; Protein; 204 AA.
AC   W23944;
DT   30-JUN-1998  (first entry)
DE   Human herpesvirus 8 interleukin-6.
KW   interleukin-6; IL-6; human herpesvirus 8; HHV8; shotgun-cloning;
KW   antibody; diagnosis; treatment.
OS   Human herpesvirus 8.
PN   WO9803657-A1.
PD   29-JAN-1998.
PF   19-JUL-1996; E03199.
PR   19-JUL-1996; WO-E03199.
PA   (BEHW ) BEHRING DIAGNOSTICS GMBH.
PA   (UYNY ) UNIV NEW YORK STATE.
PI   Albrecht J, Fleckenstein B, Friedman-kien A, Huang Y,
PI   Neipel F;
DR   WPI; 98-120781/11.
PT   Viral interleukin-6 produced recombinantly from human herpes virus 8
PT   DNA - and related nucleic acid and antibodies, used for diagnosis
PT   and treatment of herpes 8 infection or related diseases, e.g. Kaposi
PT   sarcoma
PS   Claim 2; Fig 2; 19pp; English.
CC   The interleukin-6 (IL-6) and protein W23945 derived from the sequence
CC   can be used to detect antibodies and antibodies can be used to detect
CC   IL-6.  This can be used for the diagnosis of HHV8 infection or
CC   associated diseases such as Kaposi sarcoma or kidney cell carcinoma.
CC   Antibodies, proteins and the gene sequence can all be used in the
CC   treatment of infections and diseases as mentioned above.
SQ   Sequence   204 AA;

  Query Match          100.0%;  Score 1579;  DB 1;  Length 204;
  Best Local Similarity 100.0%;  Pred. No. 9.31e-140;
  Matches   204;  Conservative    0;  Mismatches   0;  Indels   0;  Gaps   0;

Db       1 MCWFKLWSLLLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy       1 MCWFKLWSLLLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60

Db      61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy      61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120

Db     121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy     121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180

Db     181 EKFAGQAVRVLDSIPDVTPDVHDK 204
           |||||||||||||||||||||||||
Qy     181 EKFAGQAVRVLDSIPDVTPDVHDK 204


RESULT    4
ID   W95015 standard; peptide; 185 AA.
AC   W95015;
DT   21-MAY-1999  (first entry)
DE   Kaposi's sarcoma herpes virus interleukin-6 (IL-6) polypeptide.
KW   Cytokine; interleukin-B30; IL-B30; forensic science; cell proliferation;
KW   inflammatory condition; drug screening; human; IL-6.
OS   Kaposis's sarcoma herpes virus.
PN   WO9905280-A1.
PD   04-FEB-1999.
PF   24-JUL-1998; U15423.
PR   25-JUL-1997; US-900905.
PA   (SCHE ) SCHERING CORP.
PI   Bazan JF;
DR   WPI; 99-142935/12.
PT   Newly isolated or recombinant polynucleotide encoding mammalian
PT   cytokine interleukin-B30 (IL-B30), including fragments - useful for
PT   regulating activation, development, differentiation and function of
PT   various cell types, and for diagnosing and treating conditions
PT   associated with IL-B30
PS   Disclosure; Page 11-12; 83pp; English.
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CC   This invention relates to mammalian cytokine interleukin-B30 (IL-B30)
CC   polypeptides. Host cells containing a vector comprising the IL-B30
CC   nucleic acids are used for the recombinant production of the proteins.
CC   The polynucleotides are useful for diagnosis of IL-B30 mediated
CC   conditions, and forensic science (e.g. to distinguish rodent from human,
CC   or as a marker to distinguish between different cells exhibiting
CC   differential expression or modification patterns). The IL-B30 (including
CC   fragments), together with antibodies that bind to IL-B30 are useful for
CC   teaching purposes. They are also used for treating conditions associated
CC   with abnormal physiology or development, including inflammatory
CC   conditions. The polypeptide cytokine should mediate cytokine synthesis
CC   and proliferation in cells. IL-B30 is useful for drug screening to
CC   identify compounds having binding affinity to IL-B30. The present
CC   sequence represents a Kaposis's sarcoma herpes virus IL-6.
SQ   Sequence   185 AA;

  Query Match           89.5%;  Score 1413;  DB 1;  Length 185;
  Best Local Similarity 100.0%;  Pred. No. 1.80e-123;
  Matches   185;  Conservative    0;  Mismatches   0;  Indels   0;  Gaps   0;

Db       1 TRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGICKGILEPAAIFHLKLPAIND 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy      20 TRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGICKGILEPAAIFHLKLPAIND 79

Db      61 TDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVINVDVMELLTKTLGWDIQEE 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy      80 TDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVINVDVMELLTKTLGWDIQEE 139

Db     121 LNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAMEKFAGQAVRVLDSIPDVTP 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy     140 LNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAMEKFAGQAVRVLDSIPDVTP 199

Db     181 DVHDK 185
           |||||
Qy     200 DVHDK 204


RESULT    5
ID   W02611 standard; Protein; 184 AA.
AC   W02611;
DT   24-FEB-1997  (first entry)
DE   Interleukin-6 (F74Y, Q75F, S76I, Q175I, S176R, Q183A).
KW   Interleukin-6; IL-6; human; superagonist; antagonist; superantagonist;
KW   bovine; granulocyte colony stimulating factor; bG-CSF; receptor; gp130;
KW   thrombocytopaenia; haematopoietic progenitor cell; rheumatoid arthritis;
KW   bone marrow transplantation; gene therapy; multiple myeloma; leukaemia;
KW   breast cancer; infectious disease; bone marrow progenitor cell; therapy;
KW   postmenopausal osteoporosis; systemic lupus erythematosus; hormone.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   misc_difference 74
FT                   /note= "F74Y"
FT   misc_difference 75
FT                   /note= "Q75F"
FT   misc_difference 76
FT                   /note= "S76I"
FT   misc_difference 175
FT                   /note= "Q175I"
FT   misc_difference 176
FT                   /note= "S176R"
FT   misc_difference 183
FT                   /note= "Q183A"
PN   WO9618648-A1.
PD   20-JUN-1996.
PF   13-DEC-1995; IT0216.
PR   14-DEC-1994; IT-RM0805.
PA   (RICE-) IST RICERCHE BIOL MOLECOLARE ANGELETTI.
PI   Ciliberto G,  Lahm A,  Savino R,  Toniatti C;
DR   WPI; 96-300575/30.
PT   Identifying interleukin-6 super-agonists and (super)antagonists -
PT   using a 3-dimensional model of bovine granulocyte colony stimulating
PT   factor to identify binding sites
PS   Claim 8; ; 26pp; English.
CC   W02610-W02612 represent human interleukin-6 (IL-6) mutants (see W02609
CC   for wild type sequence), with an increased specificity for the specific
CC   receptor. These sequences were identified using the method of the
CC   invention. The method comprises comparing IL-6 with the sequence of the
CC   bovine granulocyte colony stimulating factor (bG-CSF). On the basis of
CC   this comparison a 3-dimensional model of IL-6 is formulated, which allows
CC   the identification of residues that form the site of interaction with the
CC   specific receptor, and those that constitute the site of interaction with
CC   gp130. The method can be used to identify superagonists, antagonists,
CC   and superantagonists of IL-6. The IL-6 superagonists identified by this
CC   method can be used for the treatment of thrombocytopaenia, and for the ex
CC   vivo expansion of human haematopoietic progenitor cells for bone marrow
CC   transplantation and gene therapy. They can also be used for the
CC   treatment of breast cancer, leukaemia, and infectious diseases or
CC   diseases connected with disorders of bone marrow progenitor cells. The
CC   antagonists and superantagonists identified by the method (see
CC   W08476-W08478) can be used for the treatment of diseases characterised by
CC   the overproduction of IL-6, particularly multiple myeloma, rheumatoid
CC   arthritis, postmenopausal osteoporosis, and systemic lupus erythematosus.
CC   The method can also be used to identify IL-6 variants with a greater
CC   affinity for the specific receptor, or variants with a reduced or
CC   abolished affinity for gp130.
SQ   Sequence   184 AA;

  Query Match           16.8%;  Score 265;  DB 1;  Length 184;
  Best Local Similarity 28.4%;  Pred. No. 2.01e-13;
  Matches    40;  Conservative   39;  Mismatches  62;  Indels   0;  Gaps   0;

Db      41 KETCNKSNMCESSKEALAENNLNLPKMAEKDGCYFIGFNEETCLVKIITGLLEFEVYLEY 100
           :: | :: :| :  |: |  :|:|| : : | | :|||| :|| |:  |::|||| : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     101 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 160
           |   |  |      ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     161 MTTHLILRSFKEFLIRSLRAL 181
           ::  :| :   |  :::| |
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    6
ID   W92803 standard; protein; 184 AA.
AC   W92803;
DT   07-MAY-1999  (first entry)
DE   Human IL-16 mutein protein.
KW   IL-16; mutein; drug-resistance; anti-tumour drug; chemotherapy; human;
KW   inhibitor; signal transduction; cytokine; gp130; prostate carcinoma.
OS   Homo sapiens.
PN   WO9858674-A1.
PD   30-DEC-1998.
PF   19-JUN-1998; IT0169.
PR   20-JUN-1997; IT-RM0368.
PA   (RICE-) IST RICERCHE BIOL MOLECOLARE ANGELETTI.
PI   Borsellino N, Ciliberto G, D Alessandro N, Savino R,
PI   Toniatti C;
DR   WPI; 99-095359/08.
PT   New composition containing a gp130 transduction inhibitor  - with a
PT   chemotherapeutic drug, useful for treating cancers especially human
PT   prostate carcinoma
PS   Claim 7; Page 29; 40pp; English.
CC   This invention describes a novel pharmaceutical composition capable of
CC   reducing drug resistance to anti-tumour drugs and comprises at least
CC   one chemotherapeutic drug and at least one agent which inhibits signal
CC   transduction from a cytokine having gp130 as transducer. The invention
CC   is used to prepare anti-tumour drugs,  particularly for the treatment
CC   of human prostate carcinoma. This sequence represents a human IL-16
CC   mutein which is used in the method of the invention.
SQ   Sequence   184 AA;

  Query Match           16.7%;  Score 264;  DB 1;  Length 184;
  Best Local Similarity 27.7%;  Pred. No. 2.47e-13;
  Matches    39;  Conservative   39;  Mismatches  63;  Indels   0;  Gaps   0;
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Db     41 KETCNKSNMCESSKEADAFWNLNLPKMAEKDGCFYKGFNEETCLVKIITGLLEFEVYLEY 100
          :: | :: :| :  |: |: :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    101 LQNRFESSEEQARAVQMRTKDLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 160
          |   | |      ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    161 MTTHLILRSFKEFLIRSLRAL 181
          ::  :| :   |  :::| |
Qy    171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    7
ID   W07200 standard; Protein; 184 AA.
AC   W07200;
DT   22-JUL-1997  (first entry)
DE   Human interleukin 6 antagonist Sant7.
KW   interleukin 6; IL-6; gp130; binding; hIL-6 DFRD; treatment;
KW   multiple myeloma; rheumatoid arthritis; lupus erythematosus;
KW   osteoporosis.
OS   Synthetic.
FH   Key             Location/Qualifiers
FT   misc_difference 31
FT                   /note= "Asp substituted for wild type Tyr"
FT   misc_difference 35
FT                   /note= "Phe substituted for wild type Gly"
FT   misc_difference 57
FT                   /note= "Leu substituted for wild type Asp"
FT   misc_difference 59
FT                   /note= "Glu substituted for wild type Phe"
FT   misc_difference 60
FT                   /note= "Asn substituted for wild type Trp"
FT   misc_difference 75
FT                   /note= "Gln substituted for wild type Tyr"
FT   misc_difference 76
FT                   /note= "Ser substituted for wild type Lys"
FT   misc_difference 118
FT                   /note= "Arg substituted for wild type Ser"
FT   misc_difference 175
FT                   /note= "Gln substituted for wild type Ile"
FT   misc_difference 176
FT                   /note= "Ser substituted for wild type Arg"
FT   misc_difference 183
FT                   /note= "Gln substituted for wild type Ala"
PN   WO9634104-A1.
PD   31-OCT-1996.
PF   26-APR-1996; IT0084.
PR   28-APR-1995; IT-RM0273.
PA   (RICE-) IST RICERCHE BIOL MOLECOLARE ANGELETTI.
PI   Ciliberto G,  Paonessa G,  Savino R;
DR   WPI; 96-497635/49.
DR   N-PSDB; T44359.
PT   New human interleukin-6 antagonists - incapable of binding gp 130,
PT   used for treating e.g. multiple myeloma, arthritis or osteoporosis
PS   Claim 1; Page 21-22; 30pp; English.
CC   The present sequence is Sant7, a human interleukin-6 (hIL-6) antagonist.
CC   Sant7 and other hIL-6 antagonists (W07197-199) are characterised in that
CC   they are totally incapable of binding gp130. Mutations were introduced
CC   into four codons in the region coding for hIL-6 cloned into
CC   pT7.7/IL-6/DFRD/Hind, creating the following amino acid substitutions:
CC   Y31D, G35F, S118R and V121D. These mutations drastically reduced the
CC   biological activity of the cytokine, without altering its ability to bind
CC   to the hIL-6 receptor, thus generating hIL-6 DFRD (see W07201). Sant7 was
CC   generated from Sant5 (contg. 5 extra mutations: Q75Y, S76K, Q175I, S176R
CC   and Q183A) by inserting 3 more amino acid substitutions: L57D, E59F and
CC   N60W. The hIL-6 antagonists can be used for the prepn. of pharmaceutical
CC   cpds. for the treatment of multiple myeloma, rheumatoid arthritis, lupus
CC   erythematosus and osteoporosis.
SQ   Sequence   184 AA;

  Query Match          16.7%;  Score 264;  DB 1;  Length 184;
  Best Local Similarity  27.7%;  Pred. No. 2.47e-13;
  Matches   39;  Conservative   39;  Mismatches  63;  Indels   0;  Gaps   0;

Db     41 KETCNKSNMCESSKEADAFWNLNLPKMAEKDGCFYKGFNEETCLVKIITGLLEFEVYLEY 100
          :: | :: :| :  |: |: :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    101 LQNRFESSEEQARAVQMRTKDLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 160
          |   | |  .   ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    161 MTTHLILRSFKEFLIRSLRAL 181
          ::  :| :   |  :::| |
Qy    171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    8
ID   W08477 standard; Protein; 184 AA.
AC   W08477;
DT   24-FEB-1997  (first entry)
DE   Interleukin-6 variant #2.
KW   Interleukin-6; IL-6; human; superagonist; antagonist; superantagonist;
KW   bovine; granulocyte colony stimulating factor; bG-CSF; receptor; gp130;
KW   thrombocytopaenia; haematopoietic progenitor cell; rheumatoid arthritis;
KW   bone marrow transplantation; gene therapy; multiple myeloma; leukaemia;
KW   breast cancer; infectious disease; bone marrow progenitor cell; therapy;
KW   postmenopausal osteoporosis; systemic lupus erythematosus; hormone.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   misc_difference 31
FT                   /note= "Y31D"
FT   misc_difference 35
FT                   /note= "G35F"
FT   misc_difference 74
FT                   /note= "F74Y"
FT   misc_difference 75
FT                   /note= "Q75Y"
FT   misc_difference 76
FT                   /note= "S76I"
FT   misc_difference 118
FT                   /note= "S118R"
FT   misc_difference 121
FT                   /note= "V121D"
FT   misc_difference 175
FT                   /note= "Q175I"
FT   misc_difference 176
FT                   /note= "S176R"
FT   misc_difference 183
FT                   /note= "Q183A"
PN   WO9618648-A1.
PD   20-JUN-1996.
PF   13-DEC-1995; IT0216.
PR   14-DEC-1994; IT-RM0805.
PA   (RICE-) IST RICERCHE BIOL MOLECOLARE ANGELETTI.
PI   Ciliberto G,  Lahm A,  Savino R,  Toniatti C;
DR   WPI; 96-300575/30.
PT   Identifying interleukin-6 super-agonists and (super)antagonists -
PT   using a 3-dimensional model of bovine granulocyte colony stimulating
PT   factor to identify binding sites
PS   Claim 10; ; 26pp; English.
CC   W08476-W08478 represent human interleukin-6 (IL-6) mutants (see W02609
CC   for wild type sequence), with greater affinity for the receptor, which
CC   can be used as IL-6 antagonists and superantagonists.  These sequences
CC   were identified using the method of the invention.  The method comprises
CC   comparing IL-6 with the bovine granulocyte colony stimulating factor
CC   (bG-CSF) sequence.  On the basis of this comparison a 3-dimensional model
CC   of IL-6 is formulated, which allows the identification of residues that
CC   form the site of interaction with the specific receptor, and those that
CC   constitute the site of interaction with gp130.  The method can be used to
CC   identify superagonists, antagonists, and superantagonists of IL-6.  The
CC   IL-6 superagonists identified by this method can be used for the
CC   treatment of thrombocytopaenia, and for the ex vivo expansion of human
CC   haematopoietic progenitor cells for bone marrow transplantation and gene
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CC   therapy.  They can also be used for the treatment of breast cancer,
CC   leukaemia, and infectious diseases or diseases connected with disorders
CC   of bone marrow progenitor cells.  The antagonists and superantagonists
CC   identified by the method can be used for the treatment of diseases
CC   characterised by the overproduction of IL-6, particularly multiple
CC   myeloma, rheumatoid arthritis, postmenopausal osteoporosis, and systemic
CC   lupus erythematosus.  The method can also be used to identify IL-6
CC   variants with a greater affinity for the specific receptor (see
CC   W02610-W02612), or variants with a reduced or abolished affinity for
CC   gp130.
SQ   Sequence   184 AA;

  Query Match           16.7%;  Score 264;  DB 1;  Length 184;
  Best Local Similarity  28.4%;  Pred. No. 2.47e-13;
  Matches    40;  Conservative   39;  Mismatches  62;  Indels   0;  Gaps   0;

Db     41 KETCNKSNMCESSKEALAENNLNLPKMAEKDGCYFIGFNEETCLVKIITGLLEFEVYLEY 100
           :: | :: :| :  |: |  :|:|| : : | | :|||||  :|| |:  |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    101 LQNRFESSEEQARAVQMRTKDLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 160
          |   | |      ::: || |   :|   ::|     : | : :|| :||: : |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    161 MTTHLILRSFKEFLIRSLRAL 181
           ::  :| :   |  :::| |
Qy    171 FASFYVLSAMEKFAGQAVRVL 191


RESULT   9
ID   W58519 standard; protein; 184 AA.
AC   W58519;
DT   28-AUG-1998  (first entry)
DE   Human interleukin 6 mutant with superantagonist activity Sant7.
KW   Human; interleukin 6; IL-6; hIL-6; superantagonist; Sant1; Sant7;
KW   mutant; adenoviral vector; multiple myeloma; Castleman's disease;
KW   mesangial glomerulonephritis; osteoporosis; rheumatoid arthritis.
OS   Synthetic.
OS   Homo sapiens.
PN   WO9813383-A1.
PD   02-APR-1998.
PF   24-SEP-1997; IT0231.
PR   24-SEP-1996; IT-M00650.
PA   (CNRS ) CNRS CENT NAT RECH SCI.
PA   (RICE-) IST RICERCHE BIOL MOLECOLARE ANGELETTI.
PI   Ciliberto G, Perricaudet M, Saggio I, Savino R;
DR   WPI; 98-230636/20.
PT   Recombinant defective adenovirus encoding antagonistic mutant of
PT   human interleukin-6 - is used to treat excessive production of this
PT   cytokine and to prolong expression of therapeutic protein from
PT   adenoviral gene therapy vectors
PS   Claim 4; Page -; 19pp; English.
CC   New recombinant defective adenovirus vector have been developed which
CC   contain at least 1 DNA sequence encoding a mutant form of human
CC   interleukin-6 (hIL-6), or its fragment or derivative, that has
CC   antagonist or superantagonist activity against hIL-6. The present
CC   sequence represents a mutant hIL-6 with superantagonist activity having
CC   the mutations: Y31D, G35F, L57D, E59F, N60W, Q75Y, S76K, S118R, V121D,
CC   Q175I, S176R and Q183A designated Sant7. The DNA sequence is placed
CC   under control of elements that provide expression in selected cell
CC   types, particularly the Rous sarcoma virus promoter. The adenovirus
CC   vector can be used to treat and/or prevent conditions associated with
CC   overproduction of IL-6, specifically multiple myeloma, Castleman's
CC   disease, mesangial glomerulonephritis, osteoporosis, Epstein-Barr
CC   positive lymphoma, rheumatoid arthritis and systemic lupus erythematosus.
CC   Cells and implants are used to express a gene encoding a therapeutic
CC   protein. The adenovirus vector can be administered by injection,
CC   preferably as a formulation containing 104-1014 (particularly 106-1010)
CC   plaque-forming units (pfu)/ml. The adenovirus vector prolongs
CC   adenovirus-mediated expression of therapeutic genes in vivo (IL-6 is the
CC   major inflammatory cytokine produced following injection of adenovirus).
SQ   Sequence   184 AA;

  Query Match           16.7%;  Score 264;  DB 1;  Length 184;
  Best Local Similarity  27.7%;  Pred. No. 2.47e-13;
  Matches    39;  Conservative   39;  Mismatches  63;  Indels   0;  Gaps   0;

Db     41 KETCNKSNMCESSKEADAFWNLNLPKMAEKDGCFYKGFNEETCLVKIITGLLEFEVYLEY 100
           :: | :: :| :  |: |: :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    101 LQNRFESSEEQARAVQMRTKDLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 160
          |   | |      ::: || |   :|   ::|     : | : :|| :||: : |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    161 MTTHLILRSFKEFLIRSLRAL 181
           ::  :| :   |  :::| |
Qy    171 FASFYVLSAMEKFAGQAVRVL 191


RESULT   10
ID   W02610 standard; Protein; 184 AA.
AC   W02610;
DT   24-FEB-1997  (first entry)
DE   Interleukin-6 (Q75Y, S76I, Q175I, S176R, Q183A).
KW   Interleukin-6; IL-6; human; superagonist; antagonist; superantagonist;
KW   bovine; granulocyte colony stimulating factor; bG-CSF; receptor; gp130;
KW   thrombocytopaenia; haematopoietic progenitor cell; rheumatoid arthritis;
KW   bone marrow transplantation; gene therapy; multiple myeloma; leukaemia;
KW   breast cancer; infectious disease; bone marrow progenitor cell; therapy;
KW   postmenopausal osteoporosis; systemic lupus erythematosus; hormone.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   misc_difference 75
FT                   /note= "Q75Y"
FT   misc_difference 76
FT                   /note= "S76I"
FT   misc_difference 175
FT                   /note= "Q175I"
FT   misc_difference 176
FT                   /note= "S176R"
FT   misc_difference 183
FT                   /note= "Q183A"
PN   WO9618648-A1.
PD   20-JUN-1996.
PF   13-DEC-1995; IT0216.
PR   14-DEC-1994; IT-RM0805.
PA   (RICE-) IST RICERCHE BIOL MOLECOLARE ANGELETTI.
PI   Ciliberto G,  Lahm A,  Savino R,  Toniatti C;
DR   WPI; 96-300575/30.
PT   Identifying interleukin-6 super-agonists and (super)antagonists -
PT   using a 3-dimensional model of bovine granulocyte colony stimulating
PT   factor to identify binding sites
PS   Claim 8; ; 26pp; English.
CC   W02610-W02612 represent human interleukin-6 (IL-6) mutants (see W02609
CC   for wild type sequence), with an increased specificity for the specific
CC   receptor.  These sequences were identified using the method of the
CC   invention.  The method comprises comparing IL-6 with the sequence of the
CC   bovine granulocyte colony stimulating factor (bG-CSF).  On the basis of
CC   this comparison a 3-dimensional model of IL-6 is formulated, which allows
CC   the identification of residues that form the site of interaction with the
CC   specific receptor, and those that constitute the site of interaction with
CC   gp130.  The method can be used to identify superagonists, antagonists,
CC   and superantagonists of IL-6.  The IL-6 superagonists identified by this
CC   method can be used for the treatment of thrombocytopaenia, and for the ex
CC   vivo expansion of human haematopoietic progenitor cells for bone marrow
CC   transplantation and gene therapy.  They can also be used for the
CC   treatment of breast cancer, leukaemia, and infectious diseases or
CC   diseases connected with disorders of bone marrow progenitor cells.  The
CC   antagonists and superantagonists identified by the method (see
CC   W08476-W08478) can be used for the treatment of diseases characterised by
CC   the overproduction of IL-6, particularly multiple myeloma, rheumatoid
CC   arthritis, postmenopausal osteoporosis, and systemic lupus erythematosus.
CC   The method can also be used to identify IL-6 variants with a greater
CC   affinity for the specific receptor, or variants with a reduced or
CC   abolished affinity for gp130.
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SQ   Sequence   184 AA;

  Query Match           16.7%;  Score 263;  DB 1;  Length 184;
  Best Local Similarity  28.4%;  Pred. No. 3.04e-13;
  Matches    40;  Conservative   38;  Mismatches  63;  Indels   0;  Gaps   0;

Db      41 KETCNKSNMCESSKEALAENNLNLPKMAEKDGCFYIGFNEETCLVKIITGLLEFEVYLEY 100
           :: | :: :| :  |: |  :|:|| : : | |  ||||| :|| |:  |::|||| : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     101 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 160
           |   | |      ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     161 MTTHLILRSFKEFLIRSLRAL 181
           ::  :| :   |  :::| |
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT   11
ID   W08476 standard; Protein; 184 AA.
AC   W08476;
DT   24-FEB-1997  (first entry)
DE   Interleukin-6 variant #1.
KW   Interleukin-6; IL-6; human; superagonist; antagonist; superantagonist;
KW   bovine; granulocyte colony stimulating factor; bG-CSF; receptor; gp130;
KW   thrombocytopaenia; haematopoietic progenitor cell; rheumatoid arthritis;
KW   bone marrow transplantation; gene therapy; multiple myeloma; leukaemia;
KW   breast cancer; infectious disease; bone marrow progenitor cell; therapy;
KW   postmenopausal osteoporosis; systemic lupus erythematosus; hormone.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   misc_difference 31
FT                   /note= "Y31D"
FT   misc_difference 35
FT                   /note= "G35F"
FT   misc_difference 75
FT                   /note= "Q75Y"
FT   misc_difference 76
FT                   /note= "S76I"
FT   misc_difference 118
FT                   /note= "S118R"
FT   misc_difference 121
FT                   /note= "V121D"
FT   misc_difference 175
FT                   /note= "Q175I"
FT   misc_difference 176
FT                   /note= "S176R"
FT   misc_difference 183
FT                   /note= "Q183A"
PN   WO9618648-A1.
PD   20-JUN-1996.
PF   13-DEC-1995; IT0216.
PR   14-DEC-1994; IT-RM0805.
PA   (RICE-) IST RICERCHE BIOL MOLECOLARE ANGELETTI.
PI   Ciliberto G,  Lahm A,  Savino R,  Toniatti C;
DR   WPI; 96-300575/30.
PT   Identifying interleukin-6 super-agonists and (super)antagonists -
PT   using a 3-dimensional model of bovine granulocyte colony stimulating
PT   factor to identify binding sites
PS   Claim 10; ; 26pp; English.
CC   W08476-W08478 represent human interleukin-6 (IL-6) mutants (see W02609
CC   for wild type sequence), with greater affinity for the receptor, which
CC   can be used as IL-6 antagonists and superantagonists.  These sequences
CC   were identified using the method of the invention.  The method comprises
CC   comparing IL-6 with the bovine granulocyte colony stimulating factor
CC   (bG-CSF) sequence.  On the basis of this comparison a 3-dimensional model
CC   of IL-6 is formulated, which allows the identification of residues that
CC   form the site of interaction with the specific receptor, and those that
CC   constitute the site of interaction with gp130.  The method can be used to
CC   identify superagonists, antagonists, and superantagonists of IL-6.  The
CC   IL-6 superagonists identified by this method can be used for the
CC   treatment of thrombocytopaenia, and for the ex vivo expansion of human
CC   haematopoietic progenitor cells for bone marrow transplantation and gene
CC   therapy.  They can also be used for the treatment of breast cancer,
CC   leukaemia, and infectious diseases or diseases connected with disorders
CC   of bone marrow progenitor cells.  The antagonists and superantagonists
CC   identified by the method can be used for the treatment of diseases
CC   characterised by the overproduction of IL-6, particularly multiple
CC   myeloma, rheumatoid arthritis, postmenopausal osteoporosis, and systemic
CC   lupus erythematosus.  The method can also be used to identify IL-6
CC   variants with a greater affinity for the specific receptor (see
CC   W02610-W02612), or variants with a reduced or abolished affinity for
CC   gp130.
SQ   Sequence   184 AA;

  Query Match           16.6%;  Score 262;  DB 1;  Length 184;
  Best Local Similarity  28.4%;  Pred. No. 3.73e-13;
  Matches    40;  Conservative   38;  Mismatches  63;  Indels   0;  Gaps   0;

Db      41 KETCNKSNMCESSKEALAENNLNLPKMAEKDGCFYIGFNEETCLVKIITGLLEFEVYLEY 100
           :: | :: :| :  |: |  :|:|| : : | |  ||||| :|| |:  |::|||| : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     101 LQNRFESSEEQARAVQMRTKDLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 160
           |   | |      ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     161 MTTHLILRSFKEFLIRSLRAL 181
           ::  :| :   |  :::| |
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT   12
ID   R45720 standard; Protein; 185 AA.
AC   R45720;
DT   23-JUL-1994  (first entry)
DE   Full length interleukin-6 with F171L L175M mutation.
KW   IL-6; carboxy terminal mutants; muteins; proliferation;
KW   differentiation; immunotherapeutic; antiinflammatory;
KW   thrombocytopenia; chemotherapy; bone marrow transplant.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   misc_difference 171
FT                   /note= "Phe 171 mutated to Leu"
FT   misc_difference 175
FT                   /note= "Leu 175 mutated to Met"
PN   WO9402512-A.
PD   03-FEB-1994.
PF   23-JUL-1993; U06928.
PR   23-JUL-1992; US-918181.
PA   (UYNC-) UNIV NORTH CAROLINA.
PI   Fowlkes D;
DR   WPI; 94-048796/06.
DR   N-PSDB; Q55689.
PT   New carboxy terminal interleukin-6 muteins - having amino acid
PT   substns. at position 171 or 175, for use in immunotherapeutic or
PT   anti-inflammation compsns.
PS   Claim 1; Fig 4; 79pp; English.
CC   The sequence shows the full length F171L L175M mutant
CC   interleukin 6.  It has been found that mutants of IL-6 having amino
CC   acid substns. at amino acid 171 or 175 have increased activity over
CC   the wild type sequence.  The IL-6 muteins are useful in
CC   proliferation of B cells, T cells, megakaryocytes and multi-
CC   potential haematopoietic progenitor cells and they also induce
CC   various acute phase proteins in liver cells.  They are useful in
CC   immunotherapeutic and antiinflammation compsns.  They can also be
CC   used for the treatment of patients suffering from thrombocytopenia
CC   or undergoing chemotherapy or bone marrow transplant.
CC   See also R45718-39.
SQ   Sequence   185 AA;

  Query Match           16.3%;  Score 258;  DB 1;  Length 185;
  Best Local Similarity  27.7%;  Pred. No. 8.48e-13;
  Matches    39;  Conservative   38;  Mismatches  64;  Indels   0;  Gaps   0;
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Db      42 KETCNKSNMCESSKEALAENNLNLPKMAEKDGCFQSGFNEETCLVKIITGLLEFEVYLEY 101
           :: | :: :| :  |: |  :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     102 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 161
           |   | |       ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     162 MTTHLILRSLKEFMQSSLRAL 182
           ::  :| ::  |   ::| |
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT   13
ID   R45718 standard; Protein; 185 AA.
AC   R45718;
DT   23-JUL-1994  (first entry)
DE   Full length interleukin-6 with F171L mutation.
KW   IL-6; carboxy terminal mutants; muteins; proliferation;
KW   differentiation; immunotherapeutic; antiinflammatory;
KW   thrombocytopenia; chemotherapy; bone marrow transplant.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   misc_difference 171
FT                   /note= "Phe 171 mutated to Leu"
PN   WO9402512-A.
PD   03-FEB-1994.
PF   23-JUL-1993; U06928.
PR   23-JUL-1992; US-918181.
PA   (UYNC-) UNIV NORTH CAROLINA.
PI   Fowlkes D;
DR   WPI; 94-048796/06.
DR   N-PSDB; Q55689.
PT   New carboxy terminal interleukin-6 muteins - having amino acid
PT   substns. at position 171 or 175, for use in immunotherapeutic or
PT   anti-inflammation compsns.
PS   Claim 1; Fig 2; 79pp; English.
CC   The sequence shows the full length F171L mutant
CC   interleukin 6.  It has been found that mutants of IL-6 having amino
CC   acid substns. at amino acid 171 or 175 have increased activity over
CC   the wild type sequence.  The IL-6 muteins are useful in
CC   proliferation of B cells, T cells, megakaryocytes and multi-
CC   potential haematopoietic progenitor cells and they also induce
CC   various acute phase proteins in liver cells.  They are useful in
CC   immunotherapeutic and antiinflammation compsns.  They can also be
CC   used for the treatment of patients suffering from thrombocytopenia
CC   or undergoing chemotherapy or bone marrow transplant.
CC   See also R45718-39.
SQ   Sequence   185 AA;

  Query Match           16.3%;  Score 257;  DB 1;  Length 185;
  Best Local Similarity  27.7%;  Pred. No. 1.04e-12;
  Matches    39;  Conservative   38;  Mismatches  64;  Indels   0;  Gaps   0;

Db      42 KETCNKSNMCESSKEALAENNLNLPKMAEKDGCFQSGFNEETCLVKIITGLLEFEVYLEY 101
           :: | :: :| :  |: |  :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     102 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 161
           |   | |       ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     162 MTTHLILRSLKEFLQSSLRAL 182
           ::  :| ::  |   ::| |
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT   14
ID   W33643 standard; protein; 212 AA.
AC   W33643;
DT   27-APR-1998  (first entry)
DE   Human interleukin-6 (IL-6) mutein polypeptide.
KW   Interleukin-6; IL-6; mutein; antagonist; human; mutation; treatment;
KW   plasmocytoma; myeloma; osteoporosis; autoimmune disease.
OS   Synthetic.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   Peptide         1. .28
FT                   /note= "signal peptide"
FT   Protein         29. .212
FT                   /note= "mature protein"
FT   Misc_difference 82
FT                   /label= K82P
FT                   /note= "wild type Lys is replaced by Pro"
FT   Misc_difference 187
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FT                   /note= "wild type Gln is replaced by Glu"
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FT                   /label= T190P
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FT                   /label= S204R
FT                   /note= "wild type Ser is replaced by Arg"
PN   WO9738104-A1.
PD   16-OCT-1997.
PF   08-APR-1997; E01736.
PR   09-APR-1996; WO-E01506.
PA   (ISTF ) ARS APPLIED RES SYSTEMS HOLDING NV.
PI   Ehlers M, Grotzinger J, Rose-John S;
DR   WPI; 97-512721/47.
PT   New interleukin-6 mutein polypeptide - useful as IL-6 antagonist for
PT   treating e.g. plasmocytoma/myeloma, osteoporosis and neoplastic and
PT   autoimmune diseases
PS   Claim 1; Pages 15-16; 37pp; English.
CC   This is a interleukin-6 (IL-6) mutein polypeptide.  This IL-6 mutein
CC   comprises a mature protein of 184 amino acids. This polypeptide is
CC   created by point mutations on the wild-type human IL-6, at positions
CC   54, 159, 162, 170,176 of the mature human IL-6. The DNA sequence encoding
CC   this IL-6 mutein and the sequences encoding variants having the same
CC   activity resulting from the degeneracy of the genetic code or point
CC   mutations can be used to transform a host cell. The IL-6 mutein can act
CC   as IL-6 antagonist. This polypeptide and its fragments can be used for
CC   treating diseases in which IL-6 has a pathogenic action such as
CC   plasmocytoma myeloma, osteoporosis and neoplastic and autoimmune
CC   diseases.
SQ   Sequence   212 AA;

  Query Match           16.2%;  Score 256;  DB 1;  Length 212;
  Best Local Similarity  27.7%;  Pred. No. 1.28e-12;
  Matches    39;  Conservative   38;  Mismatches  64;  Indels   0;  Gaps   0;

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Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     129 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLED 188
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Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     189 MPTHLILRSLKEFLQRSLRAL 209
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Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT   15
ID   W35878 standard; protein; 212 AA.
AC   W35878;
DT   27-APR-1998  (first entry)
DE   Human interleukin-6 (IL-6) mutein polypeptide.
KW   Interleukin-6; IL-6; mutein; antagonist; human; mutation; treatment;
KW   plasmocytoma; myeloma; osteoporosis; autoimmune disease.
OS   Synthetic.
OS   Homo sapiens.
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FH   Key             Location/Qualifiers
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FT                   /note= "signal peptide"
FT   Protein         29. .212
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FT                   /label= K82P
FT                   /note= "wild type Lys is replaced by Pro"
FT   Misc_difference 187
FT                   /label= Q187E
FT                   /note= "wild type Gln is replaced by Glu"
FT   Misc_difference 190
FT                   /label= T190P
FT                   /note= "wild type Thr is replaced by Pro"
FT   Misc_difference 198
FT                   /label= F198L
FT                   /note= "wild type Phe is replaced by Leu"
FT   Misc_difference 204
FT                   /label= S204R
FT                   /note= "wild type Ser is replaced by Arg"
PN   WO9738103-A1.
PD   16-OCT-1997.
PF   09-APR-1996; E01506.
PR   09-APR-1996; WO-E01506.
PA   (ISTF ) ARS APPLIED RES SYSTEMS HOLDING NV.
PI   Ehlers M, Grotzinger J, Rose-john S;
DR   WPI; 97-512720/47.
PT   New interleukin-6 mutein polypeptides - useful as IL-6 antagonists
PT   for treating e.g. plasmocytoma/myeloma, osteoporosis and neoplastic
PT   and autoimmune diseases.
PS   Claim 1; Pages 15-16; 38pp; English.
CC   This is a interleukin-6 (IL-6) mutein polypeptide.  This IL-6 mutein
CC   comprises a mature protein of 184 amino acids. This polypeptide is
CC   created by point mutations on the wild-type human IL-6, at positions
CC   54, 159, 162, 170,176 of the mature human IL-6. The DNA sequence encoding
CC   this IL-6 mutein and the sequences encoding variants having the same
CC   activity resulting from the degeneracy of the genetic code or point
CC   mutations can be used to transform a host cell. The IL-6 mutein can act
CC   as IL-6 antagonist. This polypeptide and its fragments can be used for
CC   treating diseases in which IL-6 has a pathogenic action such as
CC   plasmocytoma myeloma, osteoporosis and neoplastic and autoimmune
CC   diseases.
SQ   Sequence   212 AA;

  Query Match           16.2%;  Score 256;  DB 1;  Length 212;
  Best Local Similarity  27.7%;  Pred. No. 1.28e-12;
  Matches    39;  Conservative   38;  Mismatches  64;  Indels   0;  Gaps   0;

Db     69 KETCNKSNMCESSPEALAENNLNLPKMAEKDGCFQSGFNEETCLVKIITGLLEFEVYLEY 128
          :: | :: :| :  |: |  :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    129 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLED 188
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Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    189 MPTHLILRSLKEFLQRSLRAL 209
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Qy    171 FASFYVLSAMEKFAGQAVRVL 191


Search completed: Fri Sep 15 16:32:05 2000
Job time : 12 secs.
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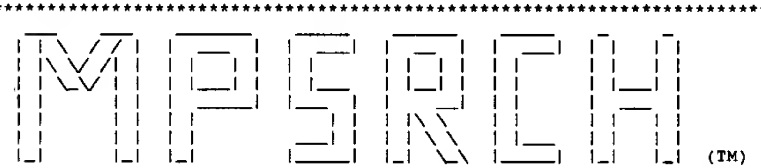

Release 3.1A John F. Collins, Biocomputing Research Unit.

MPsrch_pp protein - protein database search, using Smith-Waterman algorithm

Run on: Fri Sep 15 16:32:22 2000; MasPar time 12.71 Seconds
757.337 Million cell updates/sec

Tabular output not generated.

Title: >US-09-230-048-2
Description: (1-204) from US09230048.pep
Perfect Score: 1579
Sequence: 1 MCWFKLWSLLLVGSLLVSGT.....GQAVRVLDSIPDVTPDVHDK 204

Scoring table: PAM 150
Gap 11

Searched: 142080 seqs, 47172406 residues

Post-processing: Minimum Match 0%
Listing first 45 summaries

Database: pir64
1:pir1 2:pir2 3:pir3 4:pir4

Statistics: Mean 46.010; Variance 91.284; scale 0.504

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description	Pred. No.
1	257	16.3	212	2	I46621	prointerleukin 6 - pi	3.49e-26
2	257	16.3	212	2	I46590	interleukin 6 - pig	3.49e-26
3	252	16.0	212	1	IVHUB2	interleukin-6 precurs	2.82e-25
4	238	15.1	208	2	T09216	interleukin-6 precurs	9.30e-23
5	222	14.1	208	1	S29549	interleukin-6 - sheep	6.42e-20
6	223	14.1	211	1	ICMS6	interleukin-6 precurs	4.28e-20
7	202	12.8	208	1	A56610	interleukin-6 precurs	1.93e-16
8	189	12.0	211	2	A34247	interleukin-6 precurs	3.15e-14
9	158	10.0	207	2	I46084	interleukin 6 - cat	3.83e-09
10	112	7.1	1017	2	S67804	LRG1 protein - yeast	2.55e-02
11	111	7.0	201	2	A42247	myelomonocytic growth	3.48e-02
12	109	6.9	421	1	F48563	I7 protein - fowlpox	6.45e-02
13	108	6.8	281	2	C70411	hypothetical protein	8.75e-02
14	108	6.8	736	2	JC5495	Prox 1 protein - chic	8.75e-02
15	108	6.8	737	2	JE0269	Prox1 protein - mouse	8.75e-02
16	104	6.6	197	2	A64484	ribosomal protein S15	2.91e-01
17	104	6.6	401	2	S09626	prrB protein - Escher	2.91e-01
18	104	6.6	921	2	T01775	kinesin homolog - Ara	2.91e-01
19	104	6.6	1022	2	I53078	homeotic gene regulat	2.91e-01
20	104	6.6	1647	2	S45252	SNF2beta protein - hu	2.91e-01
21	103	6.5	318	2	C64066	transcription regulat	3.92e-01
22	102	6.5	428	2	B72118	ATPase - Chlamydia pn	5.26e-01
23	103	6.5	521	2	JS0723	cytochrome P450 ALK5-	3.92e-01
24	103	6.5	1572	2	S45251	SNF2alpha protein - h	3.92e-01
25	103	6.5	1586	2	S39580	HBRM protein - human	3.92e-01
26	101	6.4	417	2	I84434	Rhesus-like protein -	7.04e-01
27	100	6.3	280	2	C64471	hypothetical protein	9.41e-01
28	100	6.3	305	2	T16465	hypothetical protein	9.41e-01
29	99	6.3	519	2	JS0725	cytochrome P450 ALK7,	1.26e+00
30	100	6.3	2535	2	T04824	hypothetical protein	9.41e-01
31	98	6.2	519	2	JS0726	cytochrome P450 ALK8,	1.67e+00
32	96	6.1	423	2	C42511	I7L protein - vaccini	2.94e+00
33	94	6.0	207	1	D64601	phosphoserine phospha	5.14e+00
34	94	6.0	226	2	E40605	cytochrome b homolog,	5.14e+00
35	95	6.0	243	2	S73698	hypothetical protein	3.89e+00
36	95	6.0	361	2	S56488	hypothetical 39.8K pr	3.89e+00
37	95	6.0	420	2	S50652	hypothetical protein	3.89e+00
38	95	6.0	423	2	E36843	K7L protein - variola	3.89e+00
39	94	6.0	453	2	T02503	hypothetical protein	5.14e+00
40	94	6.0	579	2	S10342	hypothetical protein	5.14e+00
41	95	6.0	586	2	S44850	K12H4.1 protein - Cae	3.89e+00
42	94	6.0	597	2	S00962	hypothetical protein	5.14e+00
43	94	6.0	2708	2	T09079	probable chloroquine	5.14e+00
44	94	6.0	2819	2	T09080	probable chloroquine	5.14e+00
45	93	5.9	94	1	F64364	conserved hypothetica	6.76e+00

ALIGNMENTS

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ORGANISM #formal_name Sus scrofa domestica #common_name domestic pig
DATE 21-Feb-1997 #sequence_revision 21-Feb-1997 #text_change 16-Jul-1999
ACCESSIONS I46621
REFERENCE I46621
#authors Richards, C.; Saklatva, J.
#journal Cytokine (1991) 3:269-276
#title Molecular Cloning and Sequence of Porcine Interleukin 6 cDNA and Expression of mRNA in Synovial Fibroblasts In Vitro.
#cross-references MUID:91338547
#accession I46621
##status preliminary; translated from GB/EMBL/DDBJ
##molecule_type mRNA
##residues 1-212 ##label RIC
##cross-references GB:M86722; NID:g164624; PIDN:AAC37333.1; PID:g164625
GENETICS
#gene IL6
CLASSIFICATION #superfamily interleukin-6
SUMMARY #length 212 #molecular-weight 23880 #checksum 819

Query Match 16.3%; Score 257; DB 2; Length 212;
Best Local Similarity 25.5%; Pred. No. 3.49e-26;
Matches 36; Conservative 47; Mismatches 58; Indels 0; Gaps 0;

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Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

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Qy     171 FASFYVLSAMEKFAGQAVRVL 191
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RESULT 2
ENTRY I46590 #type complete
TITLE interleukin 6 - pig
ORGANISM #formal_name Sus scrofa domestica #common_name domestic pig
DATE 21-Feb-1997 #sequence_revision 21-Feb-1997 #text_change 16-Jul-1999
ACCESSIONS I46590

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REFERENCE        I46590
  #authors       Mathialagan, N.; Bixby, J.; Roberts, M.R.
  #journal       Mol. Reprod. Dev. (1992) 32:324-330
  #title         Expression of interleukin-6 in porcine, ovine, and bovine
                   preimplantation conceptuses.
  #cross-references MUID:92360284
  #accession     I46590
    ##status          preliminary; translated from GB/EMBL/DDBJ
    ##molecule_type mRNA
    ##residues       1-212 ##label MAT
    ##cross-references GB:M80258; NID:g164514; PIDN:AAC27127.1; PID:g164515
GENETICS
  #gene          IL-6
CLASSIFICATION   #superfamily interleukin-6
SUMMARY          #length 212  #molecular-weight 23952  #checksum 759

  Query Match             16.3%;  Score 257;  DB 2;  Length 212;
  Best Local Similarity   25.5%;  Pred. No. 3.49e-26;
  Matches    36;  Conservative    47;  Mismatches  58;  Indels   0;  Gaps   0;

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Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGPFEFEVLFKF 110

Db     129 LQKEYESNKGNVEAVQISTKALIQTLRQKGKNPDKATTPNPTTNAGLLDKLQSQNEWMKN 188
           |  |:  :  ||: ::: ||:|   :::  ::  |:  : |  : ||| :||: : |:::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     189 TKIILILRSLEDFLQFSLRAI 209
             : :| ::| |   ::| :
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    3
ENTRY            IVHUB2     #type complete
TITLE            interleukin-6 precursor - human
ALTERNATE_NAMES  B-cell differentiation factor; B-cell hybridoma growth
                   factor; B-cell stimulating factor 2 (BSF-2); CTL
                   differentiation factor; IL-6; interferon beta-II-a;
                   megakaryocyte potentiation factor
ORGANISM         #formal_name Homo sapiens #common_name man
DATE             28-Dec-1987 #sequence_revision 28-Dec-1987 #text_change
                   22-Jun-1999
ACCESSIONS       A32648; A25692; A26966; A33515; A25801; A25921; I52193;
                   I56003; A27601; B27601; A60400; A29085; A61159; A61462;
                   A48419; C48419; B48419; JX0305; S04982
REFERENCE        A32648
  #authors       Yasukawa, K.; Hirano, T.; Watanabe, Y.; Muratani, K.;
                   Matsuda, T.; Nakai, S.; Kishimoto, T.
  #journal       EMBO J. (1987) 6:2939-2945
  #title         Structure and expression of human B cell stimulatory factor-2
                   (BSF-2/IL-6) gene.
  #cross-references MUID:88082664
  #accession     A32648
    ##molecule_type DNA
    ##residues       1-212 ##label YAS
    ##cross-references GB:Y00081; NID:g29494; PIDN:CAA68278.1; PID:g29495
    ##note          the authors translated the codon CAG for residue 130 as
                     Glu
REFERENCE        A91051
  #authors       Zilberstein, A.; Ruggieri, R.; Korn, J.H.; Revel, M.
  #journal       EMBO J. (1986) 5:2529-2537
  #title         Structure and expression of cDNA and genes for human
                   interferon-beta-2, a distinct species inducible by
                   growth-stimulatory cytokines.
  #cross-references MUID:87053818
  #accession     A25692
    ##molecule_type mRNA
    ##residues       1-212 ##label ZIL
    ##cross-references GB:X04430; NID:g32673; PIDN:CAA28026.1; PID:g32674
REFERENCE        A93387
  #authors       Hirano, T.; Yasukawa, K.; Harada, H.; Taga, T.; Watanabe, Y.;
                   Matsuda, T.; Kashiwamura, S.I.; Nakajima, K.; Koyama, K.;
                   Iwamatsu, A.; Tsunasawa, S.; Sakiyama, F.; Matsui, H.;
                   Takahara, Y.; Taniguchi, T.; Kishimoto, T.
  #journal       Nature (1986) 324:73-76
  #title         Complementary DNA for a novel human interleukin (BSF-2) that
                   induces B lymphocytes to produce immunoglobulin.
  #cross-references MUID:87065033
  #accession     A26966
    ##molecule_type mRNA
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    ##cross-references GB:X04602; NID:g33849; PIDN:CAA28268.1; PID:g33850
REFERENCE        A33515
  #authors       Tonouchi, N.; Miwa, K.; Karasuyama, H.; Matsui, H.
  #journal       Biochem. Biophys. Res. Commun. (1989) 163:1056-1062
  #title         Deletion of 3' untranslated region of human BSF-2 mRNA causes
                   stabilization of the mRNA and high-level expression in
                   mouse NIH3T3 cells.
  #cross-references MUID:89391958
  #accession     A33515
    ##molecule_type mRNA
    ##residues       1-212 ##label TON
    ##cross-references GB:M29150; NID:g186349; PIDN:AAA59154.1; PID:g307063
REFERENCE        A25801
  #authors       Haegeman, G.; Content, J.; Volckaert, G.; Derynck, R.;
                   Tavernier, J.; Fiers, W.
  #journal       Eur. J. Biochem. (1986) 159:625-632
  #title         Structural analysis of the sequence coding for an inducible
                   26-kDa protein in human fibroblasts.
  #cross-references MUID:87004683
  #accession     A25801
    ##molecule_type DNA; mRNA
    ##residues       1-212 ##label HAE
    ##cross-references GB:X04403
    ##experimental_source fibroblast
REFERENCE        A25921
  #authors       May, L.T.; Helfgott, D.C.; Sehgal, P.B.
  #journal       Proc. Natl. Acad. Sci. U.S.A. (1986) 83:8957-8961
  #title         Anti-beta-interferon antibodies inhibit the increased
                   expression of HLA-B7 mRNA in tumor necrosis factor-treated
                   human fibroblasts: structural studies of the beta-2
                   interferon involved.
  #cross-references MUID:87067433
  #accession     A25921
    ##molecule_type mRNA
    ##residues       1-212 ##label MAY
    ##cross-references GB:M14584; NID:g184628; PIDN:AAA52728.1; PID:g306910
REFERENCE        I52193
  #authors       Wong, G.G.; Witek-Giannotti, J.; Hewick, R.M.; Clark, S.C.;
                   Ogawa, M.
  #journal       Behring Inst. Mitt. (1988) 83:40-47
  #title         Interleukin 6: Identification as a hematopoietic
                   colony-stimulating factor.
  #cross-references MUID:89193317
  #accession     I52193
    ##status          preliminary; translated from GB/EMBL/DDBJ
    ##molecule_type mRNA
    ##residues       1-212 ##label WON
    ##cross-references GB:M54894; NID:g186351; PIDN:AAC41704.1; PID:g186352
REFERENCE        I56003
  #authors       Brakenhoff, J.P.; de Groot, E.R.; Evers, R.F.; Pannekoek, H.;
                   Aarden, L.A.
  #journal       J. Immunol. (1987) 139:4116-4121
  #title         Molecular cloning and expression of hybridoma growth factor
                   in Escherichia coli.
  #cross-references MUID:88088768
  #accession     I56003
    ##status          translated from GB/EMBL/DDBJ
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    ##residues       1-212 ##label BRA
    ##cross-references GB:M18403; NID:g184631; PIDN:AAA52729.1; PID:g306911
REFERENCE        A92816
  #authors       Van Damme, J.; Van Beeumen, J.; Decock, B.; Van Snick, J.; De
                   Ley, M.; Billiau, A.
  #journal       J. Immunol. (1988) 140:1534-1541
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   #title        Separation and comparison of two monokines with
                   lymphocyte-activating factor activity: IL-1-beta and
                   hybridoma growth factor (HGF). Identification of
                   leukocyte-derived HGF as IL-6.
   #cross-references MUID:88154445
   #accession    A27601
      ##molecule_type protein
      ##residues      28-51,'X',53-57,'X',59,'X',61 ##label VAN1
   #accession    B27601
      ##molecule_type protein
      ##residues      30-56,'XX',59-61,'X',63 ##label VA2
REFERENCE        A60400
   #authors      Yamamoto, R.; Lin, L.S.; Lowe, R.; Warren, M.K.; White, T.J.
   #journal      J. Immunol. (1990) 144:1808-1816
   #title        The human lung fibroblast cell line, MRC-5, produces multiple
                   factors involved with megakaryocytopoiesis.
   #cross-references MUID:90171574
   #accession    A60400
      ##molecule_type protein
      ##residues      30-43 ##label YAM
REFERENCE        A29085
   #authors      Hirano, T.; Taga, T.; Yasukawa, K.; Nakajima, K.; Nakano, N.;
                   Takatsuki, F.; Shimizu, M.; Murashima, A.; Tsunasawa, S.;
                   Sakiyama, F.; Kishimoto, T.
   #journal      Proc. Natl. Acad. Sci. U.S.A. (1987) 84:228-231
   #title        Human beta-cell differentiation factor defined by an
                   anti-peptide antibody and its possible role in autoantibody
                   production.
   #cross-references MUID:87092370
   #accession    A29085
      ##molecule_type protein
      ##residues      29-42 ##label HIR2
REFERENCE        A61159
   #authors      Noda, M.; Takeda, K.; Sugimoto, H.; Hosoi, T.; Takechi, K.;
                   Hara, T.; Ishikawa, H.; Arimura, H.; Konno, K.
   #journal      Anticancer Res. (1991) 11:961-968
   #title        Purification and characterization of human fibroblast derived
                   differentiation inducing factor for human monoblastic
                   leukemia cells identical to interleukin-6.
   #cross-references MUID:91290785
   #accession    A61159
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REFERENCE        A61462
   #authors      Ming, J.E.; Cernetti, C.; Steinman, R.M.; Granelli-Piperno,
                   A.
   #journal      J. Mol. Cell. Immunol. (1989) 4:203-212
   #title        Interleukin 6 is the principal cytolytic T lymphocyte
                   differentiation factor for thymocytes in human leukocyte
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   #cross-references MUID:90121567
   #accession    A61462
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      ##residues      28-48 ##label MIN
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REFERENCE        A48419
   #authors      May, L.T.; Shaw, J.E.; Khanna, A.K.; Zabriskie, J.B.; Sehgal,
                   P.B.
   #journal      Cytokine (1991) 3:204-211
   #title        Marked cell-type-specific differences in glycosylation of
                   human interleukin-6.
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   #accession    A48419
      ##molecule_type protein
      ##residues      30-37,'X',39-40 ##label MAY2
      ##experimental_source FS-4 fibroblasts
      ##note          sequence extracted from NCBI backbone
      ##note          this 28-30K form contained both N-linked and O-linked
                       carbohydrate; a 25K form containing only N-linked
                       carbohydrate was also found
   #accession    C48419
      ##molecule_type protein
      ##residues      28-40 ##label MAY3
      ##experimental_source FS-4 fibroblasts
      ##note          sequence extracted from NCBI backbone (NCBIP:63787)
      ##note          this 23-25K form contained O-linked but not N-linked
                       carbohydrate
REFERENCE        JX0305
   #authors      Orita, T.; Oheda, M.; Hasegawa, M.; Kuboniwa, H.; Esaki, K.;
                   Ochi, N.
   #journal      J. Biochem. (1994) 115:345-350
   #title        Polypeptide and carbohydrate structure of recombinant human
                   interleukin-6 produced in chinese hamster ovary cells.
   #cross-references MUID:94266765
   #contents     annotation; modified sites in recombinant protein from CHO
                   cells
REFERENCE        S04981
...
Note: remainder of annotations omitted.

  Query Match           16.0%;  Score 252;  DB 1;  Length 212;
  Best Local Similarity  27.7%;  Pred. No. 2.82e-25;
  Matches    39;  Conservative   37;  Mismatches  65;  Indels   0;  Gaps   0;

Db      69 KETCNKSNMCESSKEALAENNLNLPKMAEKDGCFQSGFNEETCLVKIITGLLEFEVYLEY 128
           :: | :: :| :  |: |  :|:|| : : | |   ||||  :|| |:  |::|||| : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     129 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 188
           |   | |       ::: || |   :|   ::|      : |  : :|| :||: : |::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     189 MTTHLILRSFKEFLQSSLRAL 209
            ::  :| : .|   ::| |
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    4
ENTRY            T09216     #type complete
TITLE            interleukin-6 precursor - horse
ORGANISM         #formal_name Equus caballus #common_name domestic horse
DATE             11-Jun-1999 #sequence_revision 11-Jun-1999 #text_change
                   23-Jul-1999
ACCESSIONS       T09216
REFERENCE        Z16613
   #authors      Swiderski, C.E.; Horohov, D.W.
   #submission   submitted to the EMBL Data Library, July 1996
   #accession    T09216
      ##status        preliminary; translated from GB/EMBL/DDBJ
      ##molecule_type mRNA
      ##residues      1-208 ##label SWI
      ##cross-references EMBL:U64794; NID:g2654387; PID:g2654388
GENETICS
   #gene         IL-6
CLASSIFICATION   #superfamily interleukin-6
KEYWORDS         cytokine; growth factor
SUMMARY          #length 208  #molecular-weight 23419  #checksum 3370

  Query Match           15.1%;  Score 238;  DB 2;  Length 208;
  Best Local Similarity  27.3%;  Pred. No. 9.30e-23;
  Matches    36;  Conservative   37;  Mismatches  58;  Indels   1;  Gaps   1;

Db      67 EMCNNFSKCENSKEVLAENNLNLPKMAEKDGCFQSGFNQETCLMKITTGLSEFQIYLEYL 126
           ::|   : |    | |  :|:|| : : | |   |||: :||:|:: |: ||:: : :|
Qy      52 DLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFL 111

Db     127 QNEFKGEKENIKTMQISTKVLV-QILMQKMKNPEVTTPDPTAKSSLLAKLHSQNEWLKNT 185
             ||     |:  |:: || |  :|  :  |       : |    :||::|:: : |:::
Qy     112 TTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHF 171

Db     186 TTHLILRSLEDF 197
           ::  :| ::| |
Qy     172 ASFYVLSAMEKF 183
```

```
RESULT    5
ENTRY             S29549     #type complete
TITLE             interleukin-6 - sheep
ORGANISM          #formal_name Ovis orientalis aries, Ovis ammon aries
                    #common_name domestic sheep
DATE              10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change
                    10-Sep-1999
ACCESSIONS        S29549
REFERENCE         S29549
   #authors       Ebrahimi, B.
   #submission    submitted to the EMBL Data Library, October 1992
   #accession     S29549
      ##status          preliminary
      ##molecule_type mRNA
      ##residues       1-208 ##label EBR
      ##cross-references EMBL:X68723
CLASSIFICATION    #superfamily interleukin-6
SUMMARY           #length 208  #molecular-weight 23526  #checksum 7927

  Query Match           14.1%;  Score 222;  DB 1;  Length 208;
  Best Local Similarity  27.1%;  Pred. No. 6.42e-20;
  Matches    36;  Conservative   37;  Mismatches  56;  Indels   4;  Gaps   4;

Db      69 KEICEKNDECENSKETLAENKLKLPKMEEKDGCFQSGFNQAVCLIKTTAGLLEYQIYLDF 128
           :::| :   |    |  |   ||||| ::: | |   |||:: || | : |::|::: : |
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     129 LQNEFE-GNQET-VMELQS-SI-RTLIQILKEKIAGLITTPATHTDLLEKMQSSNEWVKN 184
           |  ||  :  :  |||| : :: : : : |:       : |     || ::|: : ||::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     185 AKVIIILRSLENF 197
               : :| ::|:|
Qy     171 FASFYVLSAMEKF 183


RESULT    6
ENTRY             ICMS6      #type complete
TITLE             interleukin-6 precursor - mouse
ALTERNATE_NAMES   B-cell hybridoma growth factor; B-cell stimulating factor 2;
                    hepatocyte-stimulating factor; IL-6; interferon beta-II;
                    interleukin-HP1; myeloid differentiation inducer MGI-2A;
                    plasmacytoma growth factor
ORGANISM          #formal_name Mus musculus #common_name house mouse
DATE              30-Jun-1990 #sequence_revision 30-Jun-1990 #text_change
                    22-Jun-1999
ACCESSIONS        A30531; A27610; A30571; S01323; S12103; E34047; A26662;
                    A40486; A60799; S10241; S38254
REFERENCE         A30531
   #authors       Tanabe, O.; Akira, S.; Kamiya, T.; Wong, G.G.; Hirano, T.;
                    Kishimoto, T.
   #journal       J. Immunol. (1988) 141:3875-3881
   #title         Genomic structure of the murine IL-6 gene. High degree
                    conservation of potential regulatory sequences between
                    mouse and human.
   #cross-references MUID:89035525
   #accession     A30531
      ##molecule_type DNA
      ##residues       1-211 ##label TAN
      ##cross-references GB:M20572; NID:g198369; PIDN:AAA39302.1; PID:g387386
REFERENCE         A27610
   #authors       Van Snick, J.; Cayphas, S.; Szikora, J.P.; Renauld, J.C.; Van
                    Roost, E.; Boon, T.; Simpson, R.J.
   #journal       Eur. J. Immunol. (1988) 18:193-197
   #title         cDNA cloning of murine interleukin-HP1: homology with human
                    interleukin 6.
   #cross-references MUID:88166883
   #accession     A27610
      ##molecule_type mRNA
      ##residues       1-211 ##label VAN
      ##cross-references GB:X06203; NID:g52701; PIDN:CAA29560.1; PID:g52702
REFERENCE         A30571
   #authors       Mock, B.A.; Nordan, R.P.; Justice, M.J.; Kozak, C.; Jenkins,
                    N.A.; Copeland, N.G.; Clark, S.C.; Wong, G.G.; Rudikoff, S.
   #journal       J. Immunol. (1989) 142:1372-1376
   #title         The murine Il-6 gene maps to the proximal region of
                    chromosome 5.
   #cross-references MUID:89124383
   #accession     A30571
      ##molecule_type mRNA
      ##residues       5-211 ##label MOC
      ##cross-references GB:M24221; NID:g341131; PIDN:AAA68814.1; PID:g870699
REFERENCE         S01323
   #authors       Simpson, R.J.; Moritz, R.L.; Rubira, M.R.; Van Snick, J.
   #journal       Eur. J. Biochem. (1988) 176:187-197
   #title         Murine hybridoma/plasmacytoma growth factor. Complete
                    amino-acid sequence and relation to human interleukin-6.
   #cross-references MUID:88329059
   #accession     S01323
      ##molecule_type protein
      ##residues       25-166,'X',168-211 ##label SIM
      ##note           the sequence from Fig. 11 is inconsistent with that from
                        Fig. 10 in having 103-Asn
REFERENCE         S12103
   #authors       Grenett, H.E.; Fuentes, N.L.; Fuller, G.M.
   #journal       Nucleic Acids Res. (1990) 18:6455
   #title         Cloning and sequence analysis of the cDNA for murine
                    interleukin-6.
   #cross-references MUID:91057159
   #accession     S12103
      ##molecule_type mRNA
      ##residues       1-211 ##label GRE
      ##cross-references EMBL:X54542; NID:g52727; PIDN:CAA38411.1; PID:g52728
REFERENCE         A90157
   #authors       Jahnen, W.; Ward, L.D.; Reid, G.E.; Moritz, R.L.; Simpson,
                    R.J.
   #journal       Biochem. Biophys. Res. Commun. (1990) 166:139-145
   #title         Internal amino acid sequencing of proteins by in situ
                    cyanogen bromide cleavage in polyacrylamide gels.
   #cross-references MUID:90147691
   #accession     E34047
      ##molecule_type protein
      ##residues       66-69,'X',71-75;78-94;128-148 ##label JA5
REFERENCE         A26662
   #authors       Van Snick, J.; Cayphas, S.; Vink, A.; Uyttenhove, C.; Coulie,
                    P.G.; Rubira, M.R.; Simpson, R.J.
   #journal       Proc. Natl. Acad. Sci. U.S.A. (1986) 83:9679-9683
   #title         Purification and NH2-terminal amino acid sequence of a
                    T-cell-derived lymphokine with growth factor activity for
                    B-cell hybridomas.
   #cross-references MUID:87092311
   #accession     A26662
      ##molecule_type protein
      ##residues       25-39,'X',41-42,'X',44-45 ##label VSN
REFERENCE         A40486
   #authors       Chiu, C.P.; Moulds, C.; Coffman, R.L.; Rennick, D.; Lee, F.
   #journal       Proc. Natl. Acad. Sci. U.S.A. (1988) 85:7099-7103
   #title         Multiple biological activities are expressed by a mouse
                    interleukin 6 cDNA clone isolated from bone marrow stromal
                    cells.
   #cross-references MUID:89017145
   #accession     A40486
      ##molecule_type mRNA
      ##residues       1-211 ##label CHI
      ##cross-references GB:J03783; NID:g198367; PIDN:AAA39301.1; PID:g309410
REFERENCE         A60799
   #authors       Shabo, Y.; Lotem, J.; Rubinstein, M.; Revel, M.; Clark, S.C.;
                    Wolf, S.F.; Kamen, R.; Sachs, L.
   #journal       Blood (1988) 72:2070-2073
   #title         The myeloid blood cell differentiation-inducing protein
                    MGI-2A is interleukin-6.
   #cross-references MUID:89062753
   #accession     A60799
      ##molecule_type protein
      ##residues       77-98 ##label SHA
REFERENCE         S10241
```

```
   #authors      Blankenstein, T.; Qin, Z.; Li, W.; Diamantstein, T.
   #journal      J. Exp. Med. (1990) 171:965-970
   #title        DNA rearrangement and constitutive expression of the
                   interleukin 6 gene in a mouse plasmacytoma.
   #cross-references MUID:90171860
   #accession    S10241
      ##status        preliminary
      ##molecule_type DNA
      ##residues      1-6 ##label BLA
      ##cross-references EMBL:X51457; NID:g49738; PIDN:CAA35824.1; PID:g581860
REFERENCE        S38254
   #authors      Zhang, J.G.; Reid, G.E.; Moritz, R.L.; Ward, L.D.; Simpson,
                   R.J.
   #journal      Eur. J. Biochem. (1993) 217:53-59
   #title        Specific covalent modification of the tryptophan residues in
                   murine interleukin-6. Effect on biological activity and
                   conformational stability.
   #cross-references MUID:94039075
   #accession    S38254
      ##status        preliminary
      ##molecule_type protein
      ##residues      38-60;75,'X',77-79;176-203 ##label ZHA
GENETICS
   #gene         Il-6
   #map_position 5
   #introns      7/1; 68/3; 106/3; 156/3
CLASSIFICATION   #superfamily interleukin-6
KEYWORDS         Castleman's disease; cytokine; growth factor;
                   immunoregulation; lymphokine; macrophage; rheumatoid
                   arthritis
FEATURE
   1-24              #domain signal sequence #status predicted #label SIG\
   25-211            #product interleukin-6 #status experimental #label MAT
SUMMARY          #length 211  #molecular-weight 24384  #checksum 5652

  Query Match           14.1%;  Score 223;  DB 1;  Length 211;
  Best Local Similarity  26.7%;  Pred. No. 4.28e-20;
  Matches    40;  Conservative   42;  Mismatches  65;  Indels   3;  Gaps   3;

Db      58 VLWEIVEMRKELCNGNSDCMNNDDALAENNLKLPEIQRNDGCYQTGYNQEICLLKISSGL 117
           :|| | |  ::|| : |:  :: | :|||| |  | |  |:|:  || |::|:
Qy      42 MLWVIDECFRDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGF 101

Db     118 LEYHSYLEYMKNNLKDNKKDKARVLQRDTETLIHIFNQEVKDLHKIVLPTP-ISNALLTD 176
           :|:  : ::  ::  :  :  |::  | ||  : :|:: | |  : | :  :||
Qy     102 FEFEVLFKFLTTEF-GKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLL-G 159

Db     177 KLESQKEWLRTKTIQFILKSLEEFLKVTLR 206
           :|:: | |:|  :  ::| ::| |  ::|
Qy     160 RLQGLKYWVRHFASFYVLSAMEKFAGQAVR 189


RESULT    7
ENTRY            A56610     #type complete
TITLE            interleukin-6 precursor - bovine
ORGANISM         #formal_name Bos primigenius taurus #common_name cattle
DATE             10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change
                   10-Sep-1999
ACCESSIONS       A56610; S22162
REFERENCE        A56610
   #authors      Droogmans, L.; Cludts, I.; Cleuter, Y.; Kettmann, R.; Burny,
                   A.
   #journal      DNA Seq. (1992) 2:411-413
   #title        Nucleotide sequence of bovine interleukin-6 cDNA.
   #cross-references MUID:93076003
   #accession    A56610
      ##status        preliminary
      ##molecule_type mRNA
      ##residues      1-208 ##label DRO
      ##cross-references EMBL:X57317; NID:g2193; PIDN:CAA40572.1; PID:g2194
      ##experimental_source BLV induced B cell-lymphosarcoma
      ##note          sequence extracted from NCBI backbone (NCBIP:118917)
CLASSIFICATION   #superfamily interleukin-6
KEYWORDS         cytokine
SUMMARY          #length 208  #molecular-weight 23758  #checksum 8010

  Query Match           12.8%;  Score 202;  DB 1;  Length 208;
  Best Local Similarity  23.2%;  Pred. No. 1.93e-16;
  Matches    33;  Conservative   48;  Mismatches  55;  Indels   6;  Gaps   6;

Db      69 KEICEKNDECESSKETLAENKLNLPKMEEKDGCFQSGFNQAICLIRTTAGLLEYQIYLDY 128
           :::| :   | :  |  |   |:|| ::: | |   |||:: || : : |::|::: : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     129 LQNEYE-GNQE-NVRDL-RKNI-RTLIQILKQKIADLITTPAT-NTDLLEKMQSSNEWVK 183
           |  |:  :  : :| :|  | : : : : |: |::    :|:  :  || ::|: : ||:
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELN-KLTKTHYSPPKFDRGLLGRLQGLKYWVR 169

Db     184 NAKIILILRNLENFLQFSLRAI 205
           :  : :|  :|:|   ::| :
Qy     170 HFASFYVLSAMEKFAGQAVRVL 191


RESULT    8
ENTRY            A34247     #type complete
TITLE            interleukin-6 precursor - rat
ALTERNATE_NAMES  IL-6
ORGANISM         #formal_name Rattus norvegicus #common_name Norway rat
DATE             15-Jun-1990 #sequence_revision 15-Jun-1990 #text_change
                   16-Jul-1999
ACCESSIONS       A34247
REFERENCE        A34247
   #authors      Northemann, W.; Braciak, T.A.; Hattori, M.; Lee, F.; Fey,
                   G.H.
   #journal      J. Biol. Chem. (1989) 264:16072-16082
   #title        Structure of the rat interleukin 6 gene and its expression in
                   macrophage-derived cells.
   #cross-references MUID:89380206
   #accession    A34247
      ##status        preliminary
      ##molecule_type mRNA
      ##residues      1-211 ##label NOR
      ##cross-references GB:M26744; NID:g204915; PIDN:AAA77659.1; PID:g204916
CLASSIFICATION   #superfamily interleukin-6
KEYWORDS         cytokine; growth factor; immunoregulation; lymphokine;
                   macrophage
SUMMARY          #length 211  #molecular-weight 24357  #checksum 5864

  Query Match           12.0%;  Score 189;  DB 2;  Length 211;
  Best Local Similarity  25.7%;  Pred. No. 3.15e-14;
  Matches    39;  Conservative   40;  Mismatches  72;  Indels   1;  Gaps   1;

Db      55 ITYVLREILEMRKELCNGNSDCMNSDDALSENNLKLPEIQRNDGCFQTGYNQEICLLKIC 114
           :  :|: | |  ::||   : |:  :: :  :|||| |   | |  |:|:  || |:
Qy      39 LNWMLWVIDECFRDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLA 98

Db     115 SGLLEFRFYLEFVKNNLQDNKKDKARVIQSNTETLVHIFKQEIKDSYKIVLPTPTSNALL 174
           |::||   : |:  ::  :  :   |::  | ||   : :|::   |   :  |  :  |
Qy      99 DGFFEFEVLFKFLTTEFGKSVINVD-VMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGL 157

Db     175 MEKLESQKEWLRTKTIQLILKALEEFLKVTMR 206
           : :|:: | |:|  :   :| |:| |   ::|
Qy     158 LGRLQGLKYWVRHFASFYVLSAMEKFAGQAVR 189


RESULT    9
ENTRY            I46084     #type complete
TITLE            interleukin 6 - cat
ORGANISM         #formal_name Felis silvestris catus #common_name domestic cat
DATE             16-Aug-1996 #sequence_revision 16-Aug-1996 #text_change
                   16-Jul-1999
ACCESSIONS       I46084
REFERENCE        I46084
   #authors      Bradley, W.G.; Gibbs, C.; Kraus, L.; Good, R.A.; Day, N.K.
   #journal      Proc. Soc. Exp. Biol. Med. (1993) 204:301-305
   #title        Molecular cloning and characterization of a cDNA encoding
```

```
                feline interleukin-6.
   #cross-references MUID:94052249
   #accession    I46084
      ##status       preliminary; translated from GB/EMBL/DDBJ
      ##molecule_type mRNA
      ##residues     1-207 ##label BRA
      ##cross-references GB:L16914; NID:g438519; PIDN:AAA16620.1; PID:g438520
CLASSIFICATION   #superfamily interleukin-6
SUMMARY          #length 207  #molecular-weight 23212  #checksum 9069

  Query Match           10.0%;  Score 158;  DB 2;  Length 207;
  Best Local Similarity  28.2%;  Pred. No. 3.83e-09;
  Matches    29;  Conservative    28;  Mismatches  43;  Indels   3;  Gaps   2;

Db      30 GPLGGDATSNRLPLTPA-DK--MEELIKYILGKISALKKEMCDNYNKCEDSKEALAENNL 86
           |:|   :|  :|| :|  :|  : : :: :|  |    :::|     |    |: |  :|
Qy      13 GSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGICKGILEPAAIFHL 72

Db      87 NLPKLAEKDGCFQSGFNQETCLTRITTGLQEFQIYLKFLQDKY 129
           :|| : : | |   |||: :|| ::: |: ||:: :|||   :
Qy      73 KLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEF 115


RESULT   10
ENTRY            S67804     #type complete
TITLE            LRG1 protein - yeast (Saccharomyces cerevisiae)
ALTERNATE_NAMES  protein D0764; protein YDL240w
ORGANISM         #formal_name Saccharomyces cerevisiae
DATE             12-Jul-1996 #sequence_revision 12-Jul-1996 #text_change
                   07-May-1999
ACCESSIONS       S67804; S43158; S47956
REFERENCE        S67798
   #authors      Alt-Moerbe, J.; Schneider, C.; Moro, M.
   #submission   submitted to the Protein Sequence Database, July 1996
   #accession    S67804
      ##molecule_type DNA
      ##residues     1-1017 ##label ALT
      ##cross-references EMBL:Z74288; NID:g1431407; PID:e253281; PID:g1431408;
                        MIPS:YDL240w
      ##experimental_source strain S288C
REFERENCE        S43158
   #authors      Mueller, A.; Xu, G.; Wells, R.; Hollenberg, C.P.;
                   Piepersberg, W.
   #submission   submitted to the EMBL Data Library, March 1994
   #description  LRG1 is expressed during sporulation in Saccharomyces
                   cerevisiae and contains motifs homologous to LIM and
                   rho/racGAP domains.
   #accession    S43158
      ##molecule_type DNA
      ##residues     1-530,'Q',532-765,'S',767-790,'T',792-820,'Q',822-837,
                      'S',839-848,'L',850-894,'F',896-927,'T',929-934,'S',
                      936-976,'TIL',980,'PPL',995,'KV',998,'QSIIPNVT'
                      ##label MUE
      ##cross-references EMBL:X78453; NID:g468734; PID:g468735
REFERENCE        S47956
   #authors      Mueller, L.; Xu, G.; Wells, R.; Hollenberg, C.P.;
                   Piepersberg, W.
   #journal      Nucleic Acids Res. (1994) 22:3151-3154
   #title        LRG1 is expressed during sporulation in Saccharomyces
                   cerevisiae and contains motifs similar to LIM and
                   rho/racGAP domains.
   #cross-references MUID:94344779
   #accession    S47956
      ##molecule_type DNA
      ##residues     28-89;98-136,'MF',139-148;157-184;419-474;755-765,'S',
                      767-790,'T',792-820,'Q',822-837,'S',839-848,'L',
                      850-894,'F',896-910 ##label MU2
      ##cross-references EMBL:X78453
GENETICS
   #gene         SGD:LRG1
      ##cross-references SGD:S0002399; MIPS:YDL240w
   #map_position 4L
CLASSIFICATION   #superfamily LIM metal-binding repeat homology
KEYWORDS         transmembrane protein
FEATURE
   28-89            #domain LIM metal-binding repeat homology #label LIM1\
   98-148           #domain LIM metal-binding repeat homology #label LIM2\
   157-184          #domain LIM metal-binding repeat homology #status
                      atypical #label LIM3\
   348-364          #domain transmembrane #status predicted #label TM1\
   419-474          #domain LIM metal-binding repeat homology #label LIM4\
   487-503          #domain transmembrane #status predicted #label TM2
SUMMARY          #length 1017  #molecular-weight 116659  #checksum 2060

  Query Match           7.1%;  Score 112;  DB 2;  Length 1017;
  Best Local Similarity  26.3%;  Pred. No. 2.55e-02;
  Matches    21;  Conservative   23;  Mismatches  33;  Indels   3;  Gaps   3;

Db     808 IQLSALLKKFIRELPQPILSTDLYELWIKAAKIDLEDEKQRVILLIYSLLPTYNRNLLEA 867
           :::  |:| :  |:  :::: |: ||  |:   |:::|  ::    ||  | ::| ||
Qy     102 FEFEVLFKFLTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSP-PKFDRGLLGR 160

Db     868 LLSFLHWTSSF-S-YIENEM 885
           | ::  |   | | |: : |
Qy     161 LQGLKYWVRHFASFYVLSAM 180


RESULT   11
ENTRY            A42247     #type complete
TITLE            myelomonocytic growth factor precursor - chicken
ALTERNATE_NAMES  colony-stimulating factor cMGF
ORGANISM         #formal_name Gallus gallus #common_name chicken
DATE             16-Feb-1994 #sequence_revision 18-Nov-1994 #text_change
                   16-Jul-1999
ACCESSIONS       A42247; S03633
REFERENCE        A42247
   #authors      Sterneck, E.; Blattner, C.; Graf, T.; Leutz, A.
   #journal      Mol. Cell. Biol. (1992) 12:1728-1735
   #title        Structure of the chicken myelomonocytic growth factor gene
                   and specific activation of its promoter in avian
                   myelomonocytic cells by protein kinases.
   #cross-references MUID:92195319
   #accession    A42247
      ##status       preliminary
      ##molecule_type DNA
      ##residues     1-201 ##label STE
      ##note         sequence extracted from NCBI backbone (NCBIN:89832,
                      NCBIP:89836)
REFERENCE        S03633
   #authors      Leutz, A.; Damm, K.; Sterneck, E.; Kowenz, E.; Ness, S.;
                   Frank, R.; Gausepohl, H.; Pan, Y.C.E.; Smart, J.; Hayman,
                   M.; Graf, T.
   #journal      EMBO J. (1989) 8:175-181
   #title        Molecular cloning of the chicken myelomonocytic growth factor
                   (cMGF) reveals relationship to interleukin 6 and
                   granulocyte colony stimulating factor.
   #cross-references MUID:89231616
   #accession    S03633
      ##molecule_type mRNA
      ##residues     1-201 ##label LEU
      ##cross-references EMBL:X14477; NID:g63596; PIDN:CAA32639.1; PID:g63597
CLASSIFICATION   #superfamily interleukin-6
KEYWORDS         glycoprotein
FEATURE
   1-23             #domain signal sequence #status predicted #label SIG\
   24-201           #product myelomonocytic growth factor #status predicted
                      #label MAT\
   123,137          #binding_site carbohydrate (Asn) (covalent) #status
                      predicted
SUMMARY          #length 201  #molecular-weight 22373  #checksum 9000

  Query Match           7.0%;  Score 111;  DB 2;  Length 201;
  Best Local Similarity  20.5%;  Pred. No. 3.48e-02;
  Matches    23;  Conservative   32;  Mismatches  53;  Indels   4;  Gaps   4;

Db      87 DQCHKRGFQAEVCFTQIRAGLHAYHDSLGAVLRL-LPNHTTLVETLQLDAANLSSNIQQQ 145
```

```
          |:|   ||    |:  :  |:  : : |   |   : :    |: ::| :  |: :||::
Qy     81 DHCGLIGFNETSCLKKLADGFFEF-EVLFKFLTTEFGKSVINVDVMELLTKTLGWDIQEE 139

Db    146 MEDLGLDTVTLPAEQRSPPPTFSG-PF-QQQVGGFFILANFQRFLETAYRAL 195
          :: |     : |  :|:     : |  :  :: ::|::|:  ::|    | | |
Qy    140 LNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAMEKFAGQAVRVL 191


RESULT   12
ENTRY            F48563     #type complete
TITLE            I7 protein - fowlpox virus (strain HP444)
ORGANISM         #formal_name fowlpox virus
DATE             17-Feb-1994 #sequence_revision 17-Feb-1994 #text_change
                   16-Jul-1999
ACCESSIONS       F48563
REFERENCE        A48563
   #authors      Binns, M.M.; Boursnell, M.E.; Skinner, M.A.
   #journal      Virus Res. (1992) 24:161-172
   #title        Gene translocations in poxviruses: the fowlpox virus
                   thymidine kinase gene is flanked by 15 bp direct repeats
                   and occupies the locus which in vaccinia virus is occupied
                   by the ribonucleotide reductase large subunit gene.
   #cross-references MUID:92410746
   #accession    F48563
      ##molecule_type DNA
      ##residues      1-421 ##label BIN
      ##cross-references GB:AJ223385; NID:g3123522; PIDN:CAA11298.1;
                          PID:e1292198; PID:g3123535
      ##note         sequence extracted from NCBI backbone (NCBIN:113549,
                      NCBIP:113555)
GENETICS
   #gene         I7
CLASSIFICATION   #superfamily vaccinia virus I7 protein
KEYWORDS         late protein
SUMMARY          #length 421  #molecular-weight 48621  #checksum 8049

  Query Match            6.9%;  Score 109;  DB 1;  Length 421;
  Best Local Similarity  36.4%;  Pred. No. 6.45e-02;
  Matches    16;  Conservative   13;  Mismatches  13;  Indels   2;  Gaps   2;

Db    282 GLNRNSYLSSLANENADIDILFNFFIDNYGVTAGCINVEVNQLL 325
          |:|  | |  ||:   ::::||:|:  ::|  :  |||:| :||
Qy     87 GFNETSCLKKLADGFFEFEVLFKFLTTEFG-KSV-INVDVMELL 128


RESULT   13
ENTRY            C70411     #type complete
TITLE            hypothetical protein aq_1286 - Aquifex aeolicus
ORGANISM         #formal_name Aquifex aeolicus
DATE             08-May-1998 #sequence_revision 08-May-1998 #text_change
                   08-May-1998
ACCESSIONS       C70411
REFERENCE        A70300
   #authors      Deckert, G.; Warren, P.V.; Gaasterland, T.; Young, W.G.;
                   Lenox, A.L.; Graham, D.E.; Overbeek, R.; Snead, M.A.;
                   Keller, M.; Aujay, M.; Huber, R.; Feldman, R.A.; Short,
                   J.M.; Olson, G.J.; Swanson, R.V.
   #journal      Nature (1998) 392:353-358
   #title        The complete genome of the hyperthermophilic bacterium
                   Aquifex aeolicus.
   #cross-references MUID:98196666
   #accession    C70411
      ##status        preliminary; nucleic acid sequence not shown;
                       translation not shown
      ##molecule_type DNA
      ##residues      1-281 ##label AQF
      ##cross-references GB:AE000732; NID:g2983704; PID:g2983716; GB:AE000657
      ##experimental_source strain VF5
GENETICS
   #gene         aq_1286
SUMMARY          #length 281  #molecular-weight 32624  #checksum 4784

  Query Match            6.8%;  Score 108;  DB 2;  Length 281;
  Best Local Similarity  35.9%;  Pred. No. 8.75e-02;
  Matches    23;  Conservative   14;  Mismatches  20;  Indels   7;  Gaps   7;

Db    170 EGLFEFLTV-FSKGKVNINTAPLLVLYSLDRDIDMELAKRI-ADYRKEKPFKQLKDLL-M 226
          | || |||  |:|: :|::   ||   :| :||: || |   : |   | | : : ||
Qy    105 EVLFKFLTTEFGKSVINVDVMELLTK-TLGWDIQEELNKLTKTHYSPPK-F-D-RGLLGR 160

Db    227 VEGM 230
          ::|:
Qy    161 LQGL 164


RESULT   14
ENTRY            JC5495     #type complete
TITLE            Prox 1 protein - chicken
ORGANISM         #formal_name Gallus gallus #common_name chicken
DATE             07-Jul-1997 #sequence_revision 29-Aug-1997 #text_change
                   17-Oct-1997
ACCESSIONS       JC5495
REFERENCE        JC5495
   #authors      Tomarev, S.I.; Sundin, O.; Banerjee-Basu, S.; Duncan, M.K.;
                   Yang, J.M.; Piatigorsky, J.
   #journal      Dev. Dyn. (1996) 206:354-367
   #title        Chicken homeobox gene Prox 1 related to Drosophila prospero
                   is expressed in the developing lens and retina.
   #cross-references MUID:97006692
   #contents     Len
   #accession    JC5495
      ##molecule_type mRNA
      ##residues      1-736 ##label TOM
      ##cross-references GB:U46563
COMMENT     This protein is involved in eye development and function.
SUMMARY          #length 736  #molecular-weight 83086  #checksum 1607

  Query Match            6.8%;  Score 108;  DB 2;  Length 736;
  Best Local Similarity  41.7%;  Pred. No. 8.75e-02;
  Matches    20;  Conservative   11;  Mismatches  12;  Indels   5;  Gaps   4;

Db    600 NML-KTYFSDVKFNRCITSQL--IK-WFSNFREFYYI-QMEKYARQAI 642
          |:| || :|  ||:| : ::|  :| | :|  || :  |||:| ||:
Qy    141 NKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAMEKFAGQAV 188


RESULT   15
ENTRY            JE0269     #type complete
TITLE            Prox1 protein - mouse
ORGANISM         #formal_name Mus musculus #common_name house mouse
DATE             05-Feb-1999 #sequence_revision 05-Feb-1999 #text_change
                   17-Mar-1999
ACCESSIONS       JE0269
REFERENCE        JE0269
   #authors      Tomarev, S.I.; Zinovieva, R.D.; Chang, B.; Hawes, N.L.
   #journal      Biochem. Biophys. Res. Commun. (1998) 248:684-689
   #title        Characterization of the mouse Prox1 gene.
   #cross-references MUID:98369610
   #accession    JE0269
      ##molecule_type mRNA
      ##residues      1-737 ##label TOM
      ##cross-references GB:AF061576
GENETICS
   #gene         Prox1
   #map_position 1
   #introns      575/3; 611/3; 676/3
SUMMARY          #length 737  #molecular-weight 83126  #checksum 4650

  Query Match            6.8%;  Score 108;  DB 2;  Length 737;
  Best Local Similarity  41.7%;  Pred. No. 8.75e-02;
  Matches    20;  Conservative   11;  Mismatches  12;  Indels   5;  Gaps   4;

Db    601 NML-KTYFSDVKFNRCITSQL--IK-WFSNFREFYYI-QMEKYARQAI 643
          |:| || :|  ||:| : ::|  :| | :|  || :  |||:| ||:
Qy    141 NKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAMEKFAGQAV 188
```

Search completed: Fri Sep 15 16:32:53 2000
Job time : 31 secs.

MPsrch_pp protein - protein database search, using Smith-Waterman algorithm

Run on: Fri Sep 15 16:33:11 2000; MasPar time 9.05 Seconds
698.860 Million cell updates/sec

Tabular output not generated.

Title: >US-09-230-048-2
Description: (1-204) from US09230048.pep
Perfect Score: 1579
Sequence: 1 MCWFKLWSLLLVGSLLVSGT.....GQAVRVLDSIPDVTPDVHDK 204

Scoring table: PAM 150
Gap 11

Searched: 85661 seqs, 30989116 residues

Post-processing: Minimum Match 0%
Listing first 45 summaries

Database: swiss-prot38
1:swissprot

Statistics: Mean 46.831; Variance 78.911; scale 0.593

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description	Pred. No.
1	262	16.6	212	1	IL6_CERTO	INTERLEUKIN-6 PRECURSO	2.95e-32
2	258	16.3	212	1	IL6_MACFA	INTERLEUKIN-6 PRECURSO	2.10e-31
3	257	16.3	212	1	IL6_PIG	INTERLEUKIN-6 PRECURSO	3.43e-31
4	256	16.2	212	1	IL6_MACMU	INTERLEUKIN-6 PRECURSO	5.60e-31
5	252	16.0	212	1	IL6_HUMAN	INTERLEUKIN-6 PRECURSO	3.96e-30
6	238	15.1	208	1	IL6_HORSE	INTERLEUKIN-6 PRECURSO	3.52e-27
7	226	14.3	205	1	IL6_ORCOR	INTERLEUKIN-6 PRECURSO	1.10e-24
8	223	14.1	211	1	IL6_MOUSE	INTERLEUKIN-6 PRECURSO	4.59e-24
9	221	14.0	208	1	IL6_CAPHI	INTERLEUKIN-6 PRECURSO	1.18e-23
10	218	13.8	208	1	IL6_SHEEP	INTERLEUKIN-6 PRECURSO	4.88e-23
11	202	12.8	208	1	IL6_BOVIN	INTERLEUKIN-6 PRECURSO	8.60e-20
12	201	12.7	209	1	IL6_PHOVI	INTERLEUKIN-6 PRECURSO	1.36e-19
13	199	12.6	207	1	IL6_MARMO	INTERLEUKIN-6 PRECURSO	3.43e-19
14	189	12.0	208	1	IL6_FELCA	INTERLEUKIN-6 PRECURSO	3.31e-17
15	189	12.0	211	1	IL6_RAT	INTERLEUKIN-6 PRECURSO	3.31e-17
16	180	11.4	207	1	IL6_CANFA	INTERLEUKIN-6 PRECURSO	1.90e-15
17	164	10.4	125	1	IL6_MUSVI	INTERLEUKIN-6 (IL-6) (	2.15e-12
18	112	7.1	1017	1	LRG1_YEAST	LRG1 PROTEIN.	2.38e-03
19	111	7.0	201	1	MGF_CHICK	MYELOMONOCYTIC GROWTH	3.41e-03
20	108	6.8	165	1	PRX1_MOUSE	HOMEOBOX PROSPERO-LIKE	9.89e-03
21	108	6.8	736	1	PRX1_CHICK	HOMEOBOX PROSPERO-LIKE	9.89e-03
22	108	6.8	736	1	PRX1_HUMAN	HOMEOBOX PROSPERO-LIKE	9.89e-03
23	104	6.6	401	1	PRRB_ECOLI	PRRB PROTEIN.	3.96e-02
24	104	6.6	1647	1	SN24_HUMAN	POSSIBLE GLOBAL TRANSC	3.96e-02
25	103	6.5	318	1	TYRR_HAEIN	TRANSCRIPTIONAL REGULA	5.58e-02
26	103	6.5	521	1	CP5I_CANMA	CYTOCHROME P450 52A9 (	5.58e-02
27	103	6.5	1586	1	SN22_HUMAN	POSSIBLE GLOBAL TRANSC	5.58e-02
28	101	6.4	416	1	RHL_MACFA	RH-LIKE PROTEIN (RHESU	1.10e-01
29	100	6.3	280	1	UPPS_METJA	PROBABLE UNDECAPRENYL	1.53e-01
30	99	6.3	519	1	CP5J_CANMA	CYTOCHROME P450 52A10	2.13e-01
31	100	6.3	850	1	DPO1_ANATH	DNA POLYMERASE I (EC 2	1.53e-01
32	98	6.2	519	1	CP5K_CANMA	CYTOCHROME P450 52A11	2.96e-01
33	96	6.1	423	1	VI07_VACCC	PROTEIN I7.	5.68e-01
34	97	6.1	3491	1	ERY1_SACER	ERYTHRONOLIDE SYNTHASE	4.11e-01
35	94	6.0	226	1	HMC5_DESVH	25.3 KDA PROTEIN IN HM	1.08e+00
36	95	6.0	243	1	Y23B_MYCPN	HYPOTHETICAL PROTEIN M	7.84e-01
37	95	6.0	361	1	YJGQ_ECOLI	HYPOTHETICAL 39.8 KDA	7.84e-01
38	95	6.0	416	1	YMG5_CAEEL	HYPOTHETICAL 47.8 KDA	7.84e-01
39	95	6.0	420	1	PEA2_YEAST	PEA2 PROTEIN (PPF2 PRO	7.84e-01
40	95	6.0	423	1	VI07_VARV	PROTEIN I7.	7.84e-01
41	95	6.0	586	1	HM26_CAEEL	HOMEOBOX PROTEIN CEH-2	7.84e-01
42	94	6.0	597	1	YKP4_KLULA	HYPOTHETICAL KILLER PL	1.08e+00
43	93	5.9	423	1	VI07_VACCV	PROTEIN I7.	1.48e+00
44	93	5.9	501	1	NU2C_MARPO	NADH-PLASTOQUINONE OXI	1.48e+00
45	93	5.9	1230	1	UBPF_YEAST	UBIQUITIN CARBOXYL-TER	1.48e+00

ALIGNMENTS

```
RESULT    1
ID   IL6_CERTO      STANDARD;      PRT;   212 AA.
AC   P46650;
DT   01-NOV-1995 (Rel. 32, Created)
DT   01-NOV-1995 (Rel. 32, Last sequence update)
DT   15-JUL-1998 (Rel. 36, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6.
OS   Cercocebus torquatus atys (Red-crowned mangabey) (Sooty mangabey).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC   Cercopithecinae; Cercocebus.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=FUJ;
RX   MEDLINE; 96003435.
RA   Villinger F.J., Brar S.S., Mayne A.E., Chikkala N., Ansari A.A.;
RT   "Comparative sequence analysis of cytokine genes from human and
RT   nonhuman primates.";
RL   J. Immunol. 155:3946-3954(1995).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS (BY SIMILARITY).
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC   ---------------------------------------------------------------------
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CC   ---------------------------------------------------------------------
DR   EMBL; L26032; AAA99972.1; -.
DR   HSSP; P05231; 1ALU.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   SIGNAL       1     29       BY SIMILARITY.
FT   CHAIN       30    212       INTERLEUKIN-6.
FT   DISULFID    72     78       POTENTIAL.
FT   DISULFID   101    111       POTENTIAL.
FT   CARBOHYD    73     73       POTENTIAL.
```

```
FT   CARBOHYD    172    172       POTENTIAL.
SQ   SEQUENCE   212 AA;  23668 MW;  C73C035226B44B9F CRC64;

  Query Match           16.6%;  Score 262;  DB 1;  Length 212;
  Best Local Similarity  28.4%;  Pred. No. 2.95e-32;
  Matches    40;  Conservative   36;  Mismatches  65;  Indels   0;  Gaps   0;

Db     69 KETCNRSNMCDSTKEALAENNLNLPKMAEKDGCFQSGFNEDTCLVKIITGLLEFEVYLEY 128
           :: | |: :| :  |: |  :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    129 LQNRFESSEEQARAVQMSTKVLIQLLQKKAKNLDAITTPEPTTNASLLTKLQAQNQWLQD 188
          |   |  |      ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    189 MTTHLILRSFKEFLQSSLRAL 209
            ::  :| :   |   ::| |
Qy    171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    2
ID   IL6_MACFA      STANDARD;      PRT;   212 AA.
AC   P79341;
DT   15-JUL-1998 (Rel. 36, Created)
DT   15-JUL-1998 (Rel. 36, Last sequence update)
DT   15-JUL-1998 (Rel. 36, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6.
OS   Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC   Cercopithecinae; Macaca.
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Tatsumi M.;
RL   Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS (BY SIMILARITY).
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; AB000554; BAA19148.1; -.
DR   HSSP; P05231; 2IL6.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   SIGNAL        1     29       BY SIMILARITY.
FT   CHAIN        30    212       INTERLEUKIN-6.
FT   DISULFID     72     78       POTENTIAL.
FT   DISULFID    101    111       POTENTIAL.
FT   CARBOHYD     73     73       POTENTIAL.
FT   CARBOHYD    172    172       POTENTIAL.
SQ   SEQUENCE   212 AA;  23654 MW;  CF8173FCBF0B0389 CRC64;

  Query Match           16.3%;  Score 258;  DB 1;  Length 212;
  Best Local Similarity  28.4%;  Pred. No. 2.10e-31;
  Matches    40;  Conservative   36;  Mismatches  65;  Indels   0;  Gaps   0;

Db     69 KETCNRSNMCESSKEALAENNLNLPKMAEKDGCFQSGFNEDTCLVKIITGLLEFEVYLEY 128
           :: | |: :| :  |: |  :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    129 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPEPTTNASLLTKLQAQNQWLQD 188
          |   |  |      ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    189 MTTHLILRSFKEFLQSSLRAL 209
            ::  :| :   |   ::| |
Qy    171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    3
ID   IL6_PIG        STANDARD;      PRT;   212 AA.
AC   P26893;
DT   01-AUG-1992 (Rel. 23, Created)
DT   01-AUG-1992 (Rel. 23, Last sequence update)
DT   15-DEC-1998 (Rel. 37, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6.
OS   Sus scrofa (Pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 91338547.
RA   Richards C., Saklatvala J.;
RT   "Molecular cloning and sequence of porcine interleukin 6 cDNA and
RT   expression of mRNA in synovial fibroblasts in vitro.";
RL   Cytokine 3:269-276(1991).
RN   [2]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 92360284.
RA   Mathialagan N., Bixby J.A., Roberts M.R.;
RT   "Expression of interleukin-6 in porcine, ovine, and bovine
RT   preimplantation conceptuses.";
RL   Mol. Reprod. Dev. 32:324-330(1992).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
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CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; M86722; AAC37333.1; -.
DR   EMBL; M80258; AAC27127.1; -.
DR   HSSP; P05231; 1ALU.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   SIGNAL        1     29       BY SIMILARITY.
FT   CHAIN        30    212       INTERLEUKIN-6.
FT   DISULFID     72     78       BY SIMILARITY.
FT   DISULFID    101    111       BY SIMILARITY.
FT   CONFLICT     30     30       G -> E (IN REF. 2).
SQ   SEQUENCE   212 AA;  23880 MW;  EF100ED030B6FDD0 CRC64;

  Query Match           16.3%;  Score 257;  DB 1;  Length 212;
  Best Local Similarity  25.5%;  Pred. No. 3.43e-31;
  Matches    36;  Conservative   47;  Mismatches  58;  Indels   0;  Gaps   0;

Db     69 KEMCEKYEKCENSKEVLAENNLNLPKMAEKDGCFQSGFNQETCLMRITTGLVEFQIYLDY 128
           :::| :   |   | |  :|:|| : : | |   |||: :|||:::: |: ||:: : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110
```

```
Db    129 LQKEYESNKGNVEAVQISTKALIQTLRQKGKNPDKATTPNPTTNAGLLDKLQSQNEWMKN 188
          |  |:  :  ||: ::: ||:|   :::  ::  |:  : |  : ||| :||: : |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    189 TKIILILRSLEDFLQFSLRAI 209
            : :| ::| |   ::| :
Qy    171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    4
ID    IL6_MACMU      STANDARD;      PRT;   212 AA.
AC    P51494;
DT    01-OCT-1996 (Rel. 34, Created)
DT    01-OCT-1996 (Rel. 34, Last sequence update)
DT    15-JUL-1998 (Rel. 36, Last annotation update)
DE    INTERLEUKIN-6 PRECURSOR (IL-6).
GN    IL6.
OS    Macaca mulatta (Rhesus macaque).
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC    Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC    Cercopithecinae; Macaca.
RN    [1]
RP    SEQUENCE FROM N.A.
RC    STRAIN=RAC 2;
RX    MEDLINE; 96003435.
RA    Villinger F.J., Brar S.S., Mayne A.E., Chikkala N., Ansari A.A.;
RT    "Comparative sequence analysis of cytokine genes from human and
RT    nonhuman primates.";
RL    J. Immunol. 155:3946-3954(1995).
CC    -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC        FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC        OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC        PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC        HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS (BY SIMILARITY).
CC    -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC    ----------------------------------------------------------------------
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CC    or send an email to license@isb-sib.ch).
CC    ----------------------------------------------------------------------
DR    EMBL; L26028; AAA99978.1; -.
DR    HSSP; P05231; 1ALU.
DR    PFAM; PF00489; IL6; 1.
DR    PRINTS; PR00433; IL6GCSFMGF.
DR    PRINTS; PR00434; INTERLEUKIN6.
DR    PROSITE; PS00254; INTERLEUKIN_6; 1.
KW    Cytokine; Glycoprotein; Growth factor; Signal.
FT    SIGNAL         1     29       BY SIMILARITY.
FT    CHAIN         30    212       INTERLEUKIN-6.
FT    DISULFID      72     78       POTENTIAL.
FT    DISULFID     101    111       POTENTIAL.
FT    CARBOHYD      73     73       POTENTIAL.
FT    CARBOHYD     172    172       POTENTIAL.
SQ    SEQUENCE   212 AA;  23728 MW;  4130DFE0CF0BCCAD CRC64;

  Query Match           16.2%;  Score 256;  DB 1;  Length 212;
  Best Local Similarity  28.4%;  Pred. No. 5.60e-31;
  Matches   40;  Conservative   35;  Mismatches  66;  Indels   0;  Gaps   0;

Db     69 KETCNRSNMCESSKEALAENNLNLPKMAEKDGCFQSGFNEDTCLVKIITGLLEFEVYLEY 128
          :: | |: :| :  |: |  :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    129 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPEPTTNASLLTKLQAQNQWLQD 188
          |  |  |      ::: || |  :|    ::|     : |   : :|| :|||:*: |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    189 MTTHLILRSFKEFLQSNLRAL 209
            ::  :| :   |    :| |
Qy    171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    5
ID    IL6_HUMAN      STANDARD;      PRT;   212 AA.
AC    P05231;
DT    13-AUG-1987 (Rel. 05, Created)
DT    13-AUG-1987 (Rel. 05, Last sequence update)
DT    15-JUL-1998 (Rel. 36, Last annotation update)
DE    INTERLEUKIN-6 PRECURSOR (IL-6) (B-CELL STIMULATORY FACTOR 2) (BSF-2)
DE    (INTERFERON BETA-2) (HYBRIDOMA GROWTH FACTOR).
GN    IL6 OR IFNB2.
OS    Homo sapiens (Human).
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC    Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
RN    [1]
RP    SEQUENCE FROM N.A., AND PARTIAL SEQUENCE.
RX    MEDLINE; 87065033.
RA    Hirano T., Yasukawa K., Harada H., Taga T., Watanabe Y., Matsuda T.,
RA    Kashiwamura S.-I., Nakajima K., Koyama K., Iwamatsu A., Tsunasawa S.,
RA    Sakiyama F., Matsui H., Takahara Y., Taniguchi T., Kishimoto T.;
RT    "Complementary DNA for a novel human interleukin (BSF-2) that induces
RT    B lymphocytes to produce immunoglobulin.";
RL    Nature 324:73-76(1986).
RN    [2]
RP    SEQUENCE FROM N.A.
RX    MEDLINE; 88082664.
RA    Yasukawa K., Hirano T., Watanabe Y., Muratani K., Matsuda T.,
RA    Nakai S., Kishimoto T.;
RT    "Structure and expression of human B cell stimulatory factor-2
RT    (BSF-2/IL-6) gene.";
RL    EMBO J. 6:2939-2945(1987).
RN    [3]
RP    SEQUENCE FROM N.A.
RX    MEDLINE; 87067433.
RA    May L.T., Helfgott D.C., Sehgal P.B.;
RT    "Anti-beta-interferon antibodies inhibit the increased expression of
RT    HLA-B7 mRNA in tumor necrosis factor-treated human fibroblasts:
RT    structural studies of the beta 2 interferon involved.";
RL    Proc. Natl. Acad. Sci. U.S.A. 83:8957-8961(1986).
RN    [4]
RP    SEQUENCE FROM N.A.
RX    MEDLINE; 87053818.
RA    Zilberstein A., Ruggieri R., Korn J.H., Revel M.;
RT    "Structure and expression of cDNA and genes for human
RT    interferon-beta-2, a distinct species inducible by growth-stimulatory
RT    cytokines.";
RL    EMBO J. 5:2529-2537(1986).
RN    [5]
RP    SEQUENCE FROM N.A.
RX    MEDLINE; 88088768.
RA    Brakenhoff J.P.J., de Groot E.R., Evers R.F., Pannekoek H.,
RA    Aarden L.A.;
RT    "Molecular cloning and expression of hybridoma growth factor in
RT    Escherichia coli.";
RL    J. Immunol. 139:4116-4121(1987).
RN    [6]
RP    SEQUENCE FROM N.A.
RX    MEDLINE; 89391958.
RA    Tonouchi N., Miwa K., Karasuyama H., Matsui H.;
RT    "Deletion of 3' untranslated region of human BSF-2 mRNA causes
RT    stabilization of the mRNA and high-level expression in mouse NIH3T3
RT    cells.";
RL    Biochem. Biophys. Res. Commun. 163:1056-1062(1989).
RN    [7]
RP    SEQUENCE FROM N.A.
RC    TISSUE=FIBROBLAST;
RX    MEDLINE; 87004683.
RA    Haegeman G., Content J., Volckaert G., Derynck R., Tavernier J.,
RA    Fiers W.;
RT    "Structural analysis of the sequence coding for an inducible 26-kDa
RT    protein in human fibroblasts.";
RL    Eur. J. Biochem. 159:625-632(1986).
```

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RN   [8]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 89193317.
RA   Wong G., Witek-Giannotti J., Hewick R., Clark S., Ogawa M.;
RT   "Interleukin 6: identification as a hematopoietic colony-stimulating
RT   factor.";
RL   Behring Inst. Mitt. 83:40-47(1988).
RN   [9]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 93178270.
RA   Chen Q.Y.;
RT   "Stable and efficient expression of human interleukin-6 cDNA in
RT   mammalian cells after gene transfer.";
RL   Chung-Hua Chung Liu Tsa Chih 14:340-344(1992).
RN   [10]
RP   SEQUENCE OF 30-63.
RX   MEDLINE; 88154445.
RA   van Damme J., van Beeumen J., Decock B., van Snick J., de Ley M.,
RA   Billiau A.;
RT   "Separation and comparison of two monokines with
RT   lymphocyte-activating factor activity: IL-1 beta and hybridoma growth
RT   factor (HGF). Identification of leukocyte-derived HGF as IL-6.";
RL   J. Immunol. 140:1534-1541(1988).
RN   [11]
RP   SEQUENCE OF 50-212 OF RECOMBINANT FORM LACKING 1ST DISULFIDE BOND.
RX   MEDLINE; 95154344.
RA   Breton J., la Fiura A., Bertolero F., Orsini G., Valsasina B.,
RA   Ziliotto R., de Filippis V., Polverino de Laureto P., Fontana A.;
RT   "Structure, stability and biological properties of a N-terminally
RT   truncated form of recombinant human interleukin-6 containing a single
RT   disulfide bond.";
RL   Eur. J. Biochem. 227:573-581(1995).
RN   [12]
RP   DISULFIDE BONDS.
RX   MEDLINE; 89286115.
RA   Clogston C.L., Boone T.C., Crandall B.C., Mendiaz E.A., Lu H.S.;
RT   "Disulfide structures of human interleukin-6 are similar to those of
RT   human granulocyte colony stimulating factor.";
RL   Arch. Biochem. Biophys. 272:144-151(1989).
RN   [13]
RP   MUTAGENESIS.
RX   MEDLINE; 91243808.
RA   Luetticken C., Kruettgen A., Moeller C., Heinrich P.C., Rose-John S.;
RT   "Evidence for the importance of a positive charge and an
RT   alpha-helical structure of the C-terminus for biological activity of
RT   human IL-6.";
RL   FEBS Lett. 282:265-267(1991).
RN   [14]
RP   STRUCTURE BY NMR.
RX   MEDLINE; 96134845.
RA   Nishimura C., Watanabe A., Gouda H., Shimada I., Arata Y.;
RT   "Folding topologies of human interleukin-6 and its mutants as studied
RT   by NMR spectroscopy.";
RL   Biochemistry 35:273-281(1996).
RN   [15]
RP   STRUCTURE BY NMR.
RX   MEDLINE; 97303053.
RA   Xu G.-Y., Yu H.-A., Hong J., Stahl M., McDonagh T., Kay L.E.,
RA   Cumming D.A.;
RT   "Solution structure of recombinant human interleukin-6.";
RL   J. Mol. Biol. 268:468-481(1997).
RN   [16]
RP   X-RAY CRYSTALLOGRAPHY (1.9 ANGSTROMS).
RX   MEDLINE; 97224126.
RA   Somers W., Stahl M., Seehra J.S.;
RT   "1.9-A crystal structure of interleukin 6: implications for a novel
RT   mode of receptor dimerization and signaling.";
RL   EMBO J. 16:989-997(1997).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC   ----------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; X04430; CAA28026.1; -.
DR   EMBL; M14584; AAA52728.1; -.
DR   EMBL; X04602; CAA28268.1; -.
DR   EMBL; Y00081; CAA68278.1; -.
DR   EMBL; M18403; AAA52729.1; -.
DR   EMBL; M29150; AAA59154.1; -.
DR   EMBL; X04402; CAA27990.1; -.
DR   EMBL; X04403; CAA27991.1; -.
DR   EMBL; M54894; AAC41704.1; -.
DR   EMBL; S56892; AAD13886.1; -.
DR   EMBL; A09363; CAA00839.1; -.
DR   PIR; A32648; IVHUB2.
DR   PIR; A25921; A25921.
DR   PDB; 1IL6; 04-FEB-98.
DR   PDB; 2IL6; 04-FEB-98.
DR   PDB; 1ALU; 03-JUN-98.
DR   MIM; 147620; -.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal; 3D-structure.
FT   SIGNAL       1    29
FT   CHAIN       30   212       INTERLEUKIN-6.
FT   DISULFID     72    78
FT   DISULFID    101   111
FT   CARBOHYD     73    73
FT   MUTAGEN     173   173       A->V: ALMOST NO LOSS OF ACTIVITY.
FT   MUTAGEN     185   185       W->R: NO LOSS OF ACTIVITY.
FT   MUTAGEN     204   204       S->P: 13% ACTIVITY.
FT   MUTAGEN     210   210       R->K,E,Q,T,A,P: LOSS OF ACTIVITY.
FT   MUTAGEN     212   212       M->T,N,S,R: LOSS OF ACTIVITY.
SQ   SEQUENCE   212 AA;  23718 MW;  1F1ED1FE1B734079 CRC64;

  Query Match           16.0%;  Score 252;  DB 1;  Length 212;
  Best Local Similarity  27.7%;  Pred. No. 3.96e-30;
  Matches    39;  Conservative   37;  Mismatches  65;  Indels   0;  Gaps   0;

Db      69 KETCNKSNMCESSKEALAENNLNLPKMAEKDGCFQSGFNEETCLVKIITGLLEFEVYLEY 128
           :: | :: :| :  |: |  :|:|| : : | |   |||| :|| |:  |::|||| : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     129 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 188
           |   | |       ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     189 MTTHLILRSFKEFLQSSLRAL 209
           ::  :| : ' |   ::| |
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    6
ID   IL6_HORSE     STANDARD;      PRT;   208 AA.
AC   Q95181; O19007; O46568;
DT   01-NOV-1997 (Rel. 35, Created)
DT   15-JUL-1999 (Rel. 38, Last sequence update)
DT   15-JUL-1999 (Rel. 38, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6.
OS   Equus caballus (Horse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Perissodactyla; Equidae; Equus.
RN   [1]
```

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RP   SEQUENCE FROM N.A.
RA   Swiderski C.E., Horohov D.W.;
RL   Submitted (DEC-1997) to the EMBL/GenBank/DDBJ databases.
RN   [2]
RP   SEQUENCE FROM N.A.
RA   Leutenegger C.M., Huder J.B., von Rechenberg B., Akens M., Auer J.;
RL   Submitted (JUL-1997) to the EMBL/GenBank/DDBJ databases.
RN   [3]
RP   SEQUENCE FROM N.A.
RA   Lai A.C.K.;
RT   "Cloning and expression of equine interleukin-6.";
RL   Submitted (JAN-1998) to the EMBL/GenBank/DDBJ databases.
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS (BY SIMILARITY).
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; U64794; AAB87703.1; -.
DR   EMBL; AF005227; AAB62246.1; -.
DR   EMBL; AF041975; AAC04574.1; -.
DR   HSSP; P05231; 1ALU.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   SIGNAL       1     27       POTENTIAL.
FT   CHAIN       28    208       INTERLEUKIN-6.
FT   DISULFID    69     75       BY SIMILARITY.
FT   DISULFID    98    108       BY SIMILARITY.
FT   CARBOHYD    71     71       POTENTIAL.
FT   CARBOHYD   184    184       POTENTIAL.
FT   CONFLICT     4      5       LS -> FF (IN REF. 1).
FT   CONFLICT     8      8       T -> A (IN REF. 3).
FT   CONFLICT   137    137       I -> V (IN REF. 2).
FT   CONFLICT   205    205       V -> I (IN REF. 3).
SQ   SEQUENCE   208 AA;  23325 MW;  A62F4C234056BF66 CRC64;

  Query Match           15.1%;  Score 238;  DB 1;  Length 208;
  Best Local Similarity  27.3%;  Pred. No. 3.52e-27;
  Matches   36;  Conservative   37;  Mismatches  58;  Indels   1;  Gaps   1;

Db      67 EMCNNFSKCENSKEVLAENNLNLPKMAEKDGCFQSGFNQETCLMKITTGLSEFQIYLEYL 126
           ::|   : |    | |  :|:|| : : | |   |||: :||:|:: |: ||:: : :|
Qy      52 DLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFL 111

Db     127 QNEFKGEKENIKTMQISTKVLV-QILMQKMKNPEVTTPDPTAKSSLLAKLHSQNEWLKNT 185
             ||    |:  |:: || |  :|  :  |     : |    :||::|:: : |:::
Qy     112 TTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHF 171

Db     186 TTHLILRSLEDF 197
           ::  :| ::| |
Qy     172 ASFYVLSAMEKF 183


RESULT    7
ID   IL6_ORCOR      STANDARD;      PRT;   205 AA.
AC   Q28747;
DT   15-FEB-2000 (Rel. 39, Created)
DT   15-FEB-2000 (Rel. 39, Last sequence update)
DT   15-FEB-2000 (Rel. 39, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6) (FRAGMENT).
GN   IL6.
OS   Orcinus orca (Killer whale).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Cetacea; Odontoceti; Delphinidae;
OC   Orcinus.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 96163018.
RA   King D.P., Schrenzel M.D., McKnight M.L., Reidarson T.H., Hanni K.D.,
RA   Stott J.L., Ferrick D.A.;
RT   "Molecular cloning and sequencing of interleukin 6 cDNA fragments from
RT   the harbor seal (Phoca vitulina), killer whale (Orcinus orca), and
RT   Southern sea otter (Enhydra lutris nereis).";
RL   Immunogenetics 43:190-195(1996).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: SECRETED.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC   ----------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; L46803; AAB01429.1; -.
DR   HSSP; P05231; 1ALU.
DR   PFAM; PF00489; IL6; 1.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   NON_TER      1      1
FT   SIGNAL      <1     21       BY SIMILARITY.
FT   CHAIN       22    205       INTERLEUKIN-6.
FT   DISULFID    64     70       BY SIMILARITY.
FT   DISULFID    93    103       BY SIMILARITY.
FT   CARBOHYD   164    164       N-LINKED (GLCNAC. . .) (POTENTIAL).
SQ   SEQUENCE   205 AA;  23266 MW;  6308F3A457960832 CRC64;

  Query Match           14.3%;  Score 226;  DB 1;  Length 205;
  Best Local Similarity  20.4%;  Pred. No. 1.10e-24;
  Matches   29;  Conservative   54;  Mismatches  58;  Indels   1;  Gaps   1;

Db      61 KEMCEKYDKCENSKEALAENNLNLPKMAEKDGCFQSGFNQETCLMRITTGLLEYQIYLDY 120
           :::| :   |    |: |  :|:|| : : | |   |||: :||:::: |:::: : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     121 LQNEYEGDKEAIEAVQISSKALAQILRQKVKNPDEVTTPDPTTNASLMNNLQSQNDDWMK 180
           |  |:       :: ::: :|:|:  ::: :::       : |  : :|:  ||: :  |::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKY-WVR 169

Db     181 NTKIILILRSLENFLQFSLRAI 202
           :   : :| ::|:|   ::| :
Qy     170 HFASFYVLSAMEKFAGQAVRVL 191


RESULT    8
ID   IL6_MOUSE      STANDARD;      PRT;   211 AA.
AC   P08505;
DT   01-AUG-1988 (Rel. 08, Created)
DT   01-AUG-1988 (Rel. 08, Last sequence update)
DT   15-JUL-1998 (Rel. 36, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6) (INTERLEUKIN HP-1) (B-CELL HYBRIDOMA
DE   GROWTH FACTOR).
GN   IL6 OR IL-6.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
RN   [1]
RP   SEQUENCE FROM N.A., AND PARTIAL SEQUENCE.
```

```
RX   MEDLINE; 88166883.
RA   van Snick J., Cayphas S., Szikora J.-P., Renauld J.-C., van Roost E.,
RA   Boon T., Simpson R.J.;
RT   "cDNA cloning of murine interleukin-HP1: homology with human
RT   interleukin 6.";
RL   Eur. J. Immunol. 18:193-197(1988).
RN   [2]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 89035525.
RA   Tanabe O., Akira S., Kamiya T., Wong G.G., Hirano T., Kishimoto T.;
RT   "Genomic structure of the murine IL-6 gene. High degree conservation
RT   of potential regulatory sequences between mouse and human.";
RL   J. Immunol. 141:3875-3881(1988).
RN   [3]
RP   SEQUENCE FROM N.A.
RC   STRAIN=BALB/C;
RX   MEDLINE; 91057159.
RA   Grenett H.E., Fuentes N.L., Fuller G.M.;
RT   "Cloning and sequence analysis of the cDNA for murine interleukin-6.";
RL   Nucleic Acids Res. 18:6455-6455(1990).
RN   [4]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 89017145.
RA   Chiu C.P., Moulds C., Coffman R.L., Rennick D., Lee F.;
RT   "Multiple biological activities are expressed by a mouse interleukin
RT   6 cDNA clone isolated from bone marrow stromal cells.";
RL   Proc. Natl. Acad. Sci. U.S.A. 85:7099-7103(1988).
RN   [5]
RP   SEQUENCE OF 5-211 FROM N.A.
RC   STRAIN=C57BL/6J;
RX   MEDLINE; 89124383.
RA   Mock B.A., Nordan R.P., Justice M.J., Kozak C., Jenkins N.A.,
RA   Copeland N.G., Clark S.C., Wong G.G., Rudikoff S.;
RT   "The murine Il-6 gene maps to the proximal region of chromosome 5.";
RL   J. Immunol. 142:1372-1376(1989).
RN   [6]
RP   SEQUENCE OF 1-6 FROM N.A.
RC   STRAIN=BALB/C;
RX   MEDLINE; 90171860.
RA   Blankenstein T., Qin Z., Li W., Diamantstein T.;
RT   "DNA rearrangement and constitutive expression of the interleukin 6
RT   gene in a mouse plasmacytoma.";
RL   J. Exp. Med. 171:965-970(1990).
RN   [7]
RP   SEQUENCE OF 25-211.
RX   MEDLINE; 88329059.
RA   Simpson R.J., Moritz R.L., Rubira M.R., van Snick J.;
RT   "Murine hybridoma/plasmacytoma growth factor. Complete amino-acid
RT   sequence and relation to human interleukin-6.";
RL   Eur. J. Biochem. 176:187-197(1988).
RN   [8]
RP   SEQUENCE OF 66-75; 78-84 AND 128-148.
RX   MEDLINE; 90147691.
RA   Jahnen W., Ward L.D., Reid G.E., Moritz R.L., Simpson R.J.;
RT   "Internal amino acid sequencing of proteins by in situ cyanogen
RT   bromide cleavage in polyacrylamide gels.";
RL   Biochem. Biophys. Res. Commun. 166:139-145(1990).
RN   [9]
RP   SEQUENCE OF 25-45.
RX   MEDLINE; 87092311.
RA   van Snick J., Cayphas S., Vink A., Uyttenhove C., Coulie P.G.,
RA   Rubira M.R., Simpson R.J.;
RT   "Purification and NH2-terminal amino acid sequence of a
RT   T-cell-derived lymphokine with growth factor activity for B-cell
RT   hybridomas.";
RL   Proc. Natl. Acad. Sci. U.S.A. 83:9679-9683(1986).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC   ---------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; X06203; CAA29560.1; -.
DR   EMBL; M20572; AAA39302.1; -.
DR   EMBL; X51457; CAA35824.1; -.
DR   EMBL; J03783; AAA39301.1; -.
DR   EMBL; X54542; CAA38411.1; -.
DR   EMBL; M24221; AAA68814.1; -.
DR   PIR; A30531; ICMS6.
DR   HSSP; P05231; 1ALU.
DR   MGD; MGI:96559; IL6.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Growth factor; Glycoprotein; Signal.
FT   SIGNAL        1     24
FT   CHAIN        25    211       INTERLEUKIN-6.
FT   DISULFID     70     76       BY SIMILARITY.
FT   DISULFID     99    109       BY SIMILARITY.
SQ   SEQUENCE   211 AA;  24384 MW;  BBB47DDA9E86787A CRC64;

  Query Match           14.1%;  Score 223;  DB 1;  Length 211;
  Best Local Similarity 26.7%;  Pred. No. 4.59e-24;
  Matches   40;  Conservative   42;  Mismatches  65;  Indels   3;  Gaps   3;

Db     58 VLWEIVEMRKELCNGNSDCMNNDDALAENNLKLPEIQRNDGCYQTGYNQEICLLKISSGL 117
          :|| | |  ::||   : |:   :: |  :||||.|   | |  |:|:  || |:: |:
Qy     42 MLWVIDECFRDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGF 101

Db    118 LEYHSYLEYMKNNLKDNKKDKARVLQRDTETLIHIFNQEVKDLHKIVLPTP-ISNALLTD 176
          :|:   : ::  ::  :   :  |::  | ||   : :|:: | |   : | :  :||
Qy    102 FEFEVLFKFLTTEF-GKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLL-G 159

Db    177 KLESQKEWLRTKTIQFILKSLEEFLKVTLR 206
          :|:: | |:|  :  ::| ::| |   ::|
Qy    160 RLQGLKYWVRHFASFYVLSAMEKFAGQAVR 189


RESULT    9
ID   IL6_CAPHI      STANDARD;      PRT;   208 AA.
AC   Q28319;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   15-JUL-1998 (Rel. 36, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6.
OS   Capra hircus (Goat).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Caprinae; Capra.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 97392354.
RA   Takakura H., Mori Y., Tatsumi M.;
RT   "Molecular cloning of caprine IL-6 cDNA and its expression in insect
RT   cells.";
RL   Int. Arch. Allergy Immunol. 113:409-416(1997).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC   ---------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------------
DR   EMBL; D86569; BAA13118.1; -.
DR   HSSP; P05231; 2IL6.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   SIGNAL        1     29       BY SIMILARITY.
FT   CHAIN        30    208       INTERLEUKIN-6.
FT   DISULFID     72     78       BY SIMILARITY.
FT   DISULFID    101    111       BY SIMILARITY.
FT   CARBOHYD     38     38       POTENTIAL.
SQ   SEQUENCE   208 AA;  23423 MW;  E92E08BF3E3230A0 CRC64;

  Query Match           14.0%;  Score 221;  DB 1;  Length 208;
  Best Local Similarity  25.5%;  Pred. No. 1.18e-23;
  Matches   36;  Conservative   42;  Mismatches  59;  Indels   4;  Gaps   4;

Db      69 KEICEKNDECENSKETLAENKLKLPKMEEKDGCFQSGFNQAICLIKTTAGLLEYQIYLDF 128
           :::| :   |   |  |  |||| ::: | |   |||:: || | : |::|::: : |
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     129 LQNEFE-GNQET-VMELQS-SI-RTLIQILKEKIAGLITTPATNTDMLEKMQSSNEWVKN 184
           |  ||   :  :  |||| : :: : : : |:      : |  :  :| ::|: : ||::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     185 AKVIIILRSLENFLQFSLRAI 205
             : :| ::|:|   ::| :
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT   10
ID   IL6_SHEEP      STANDARD;      PRT;   208 AA.
AC   P29455;
DT   01-APR-1993 (Rel. 25, Created)
DT   01-JUN-1994 (Rel. 29, Last sequence update)
DT   15-JUL-1998 (Rel. 36, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6.
OS   Ovis aries (Sheep).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Caprinae; Ovis.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 94041419.
RA   Andrews A.E., Barcham G.J., Ashman K., Meeusen E.N.T., Brandon M.R.,
RA   Nash A.D.;
RT   "Molecular cloning and characterization of a ruminant interleukin-6
RT   cDNA.";
RL   Immunol. Cell Biol. 71:341-348(1993).
RN   [2]
RP   SEQUENCE FROM N.A.
RA   Ebrahimi B.;
RL   Submitted (OCT-1992) to the EMBL/GenBank/DDBJ databases.
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC   ---------------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------------
DR   EMBL; X62501; CAA44363.1; -.
DR   EMBL; X68723; CAA48662.1; -.
DR   EMBL; A19159; CAA01443.1; -.
DR   PIR; S29549; S29549.
DR   HSSP; P05231; 2IL6.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   SIGNAL        1     29       BY SIMILARITY.
FT   CHAIN        30    208       INTERLEUKIN-6.
FT   DISULFID     72     78       BY SIMILARITY.
FT   DISULFID    101    111       BY SIMILARITY.
FT   CARBOHYD     38     38       POTENTIAL.
FT   CONFLICT      4      4       L -> R (IN REF. 2).
FT   CONFLICT    110    110       I -> V (IN REF. 2).
FT   CONFLICT    171    171       M -> L (IN REF. 2).
FT   CONFLICT    201    201       S -> R (IN REF. 2).
SQ   SEQUENCE   208 AA;  23446 MW;  EEC996C13E3230A0 CRC64;

  Query Match           13.8%;  Score 218;  DB 1;  Length 208;
  Best Local Similarity  25.5%;  Pred. No. 4.88e-23;
  Matches   36;  Conservative   41;  Mismatches  60;  Indels   4;  Gaps   4;

Db      69 KEICEKNDECENSKETLAENKLKLPKMEEKDGCFQSGFNQAICLIKTTAGLLEYQIYLDF 128
           :::| :   |  |  |  |||| ::: | |   |||:: || | : |::|::: : |
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     129 LQNEFE-GNQET-VMELQS-SI-RTLIQILKEKIAGLITTPATHTDMLEKMQSSNEWVKN 184
           |  ||   :  :  |||| : :: : : : |:      : |     :| ::|: : ||::
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     185 AKVIIILRSLENFLQFSLRAI 205
             : :| ::|:|   ::| :
Qy     171 FASFYVLSAMEKFAGQAVRVL 191


RESULT   11
ID   IL6_BOVIN      STANDARD;      PRT;   208 AA.
AC   P26892;
DT   01-AUG-1992 (Rel. 23, Created)
DT   01-AUG-1992 (Rel. 23, Last sequence update)
DT   15-JUL-1998 (Rel. 36, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6.
OS   Bos taurus (Bovine).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Bovinae; Bos.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=HOLSTEIN;
RX   MEDLINE; 93076003.
RA   Droogmans L., Cludts I., Cleuter Y., Kettmann R., Burny A.;
RT   "Nucleotide sequence of bovine interleukin-6 cDNA.";
RL   DNA Seq. 2:411-413(1992).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
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CC   ---------------------------------------------------------------------
DR   EMBL; X57317; CAA40572.1; -.
DR   PIR; S22162; S22162.
DR   HSSP; P05231; 2IL6.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   SIGNAL       1     29       BY SIMILARITY.
FT   CHAIN       30    208       INTERLEUKIN-6.
FT   DISULFID    72     78       BY SIMILARITY.
FT   DISULFID   101    111       BY SIMILARITY.
FT   CARBOHYD    38     38       POTENTIAL.
SQ   SEQUENCE   208 AA;  23758 MW;  A0F000B9BA2EC341 CRC64;

  Query Match           12.8%;  Score 202;  DB 1;  Length 208;
  Best Local Similarity  23.2%;  Pred. No. 8.60e-20;
  Matches    33;  Conservative   48;  Mismatches  55;  Indels   6;  Gaps   6;

Db      69 KEICEKNDECESSKETLAENKLNLPKMEEKDGCFQSGFNQAICLIRTTAGLLEYQIYLDY 128
           :::| :   | :  |  |   |:|| ::: | |   |||:: || : : |:::::: : :
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     129 LQNEYE-GNQE-NVRDL-RKNI-RTLIQILKQKIADLITTPAT-NTDLLEKMQSSNEWVK 183
           |  |:  :  : :| :|  | : : : : |: |::    :|:  :  || ::|: : ||:
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELN-KLTKTHYSPPKFDRGLLGRLQGLKYWVR 169

Db     184 NAKIILILRNLENFLQFSLRAI 205
           :   : :|  :|:|   ::| :
Qy     170 HFASFYVLSAMEKFAGQAVRVL 191


RESULT   12
ID   IL6_PHOVI      STANDARD;      PRT;   209 AA.
AC   Q28819;
DT   15-FEB-2000 (Rel. 39, Created)
DT   15-FEB-2000 (Rel. 39, Last sequence update)
DT   15-FEB-2000 (Rel. 39, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6) (FRAGMENT).
GN   IL6.
OS   Phoca vitulina (Harbor seal).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Carnivora; Pinnipedia; Phocidae; Phoca.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 96163018.
RA   King D.P., Schrenzel M.D., McKnight M.L., Reidarson T.H., Hanni K.D.,
RA   Stott J.L., Ferrick D.A.;
RT   "Molecular cloning and sequencing of interleukin 6 cDNA fragments from
RT   the harbor seal (Phoca vitulina), killer whale (Orcinus orca), and
RT   Southern sea otter (Enhydra lutris nereis).";
RL   Immunogenetics 43:190-195(1996).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: SECRETED.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
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CC   ---------------------------------------------------------------------
DR   EMBL; L46802; AAB01430.1; -.
DR   HSSP; P05231; 2IL6.
DR   PFAM; PF00489; IL6; 1.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   NON_TER      1      1
FT   SIGNAL      <1     26       BY SIMILARITY.
FT   CHAIN       27    209       INTERLEUKIN-6.
FT   DISULFID    69     75       BY SIMILARITY.
FT   DISULFID    98    108       BY SIMILARITY.
SQ   SEQUENCE   209 AA;  23483 MW;  75144922E43B48E9 CRC64;

  Query Match           12.7%;  Score 201;  DB 1;  Length 209;
  Best Local Similarity  22.6%;  Pred. No. 1.36e-19;
  Matches    30;  Conservative   42;  Mismatches  61;  Indels   0;  Gaps   0;

Db      66 KEMCDKYNKCEDSKEALAENNLRLPKLAEKDGCFQSGFNQETCLTRITTGLLEFQIHLKY 125
           :::| :   |.   |: |  :|:|| : : | |   |||: :|| ::: |::||:: :|:
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     126 IQANYEGNKEDANSVYISTKLLVQMLMKKVKSQDEVTTPDPTTDTSLQAILKAQDKWLKH 185
           : ::: :  : : : : || |   :   ::       : |  | :| : | :   |::|
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     186 TTIHLILRSLEDF 198
           :   :| ::| |
Qy     171 FASFYVLSAMEKF 183


RESULT   13
ID   IL6_MARMO      STANDARD;      PRT;   207 AA.
AC   O35736;
DT   15-JUL-1999 (Rel. 38, Created)
DT   15-JUL-1999 (Rel. 38, Last sequence update)
DT   15-JUL-1999 (Rel. 38, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6.
OS   Marmota monax (Woodchuck).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Sciuridae; Sciurinae;
OC   Marmota.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=PERIPHERAL BLOOD;
RX   MEDLINE; 98139533.
RA   Lohrengel B., Lu M., Roggendorf M.;
RT   "Molecular cloning of the woodchuck cytokines: TNF-alpha, IFN-gamma,
RT   and IL-6.";
RL   Immunogenetics 47:332-335(1998).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS (BY SIMILARITY).
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC   ---------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; Y14139; CAA74571.1; -.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   SIGNAL       1     18       POTENTIAL.
FT   CHAIN       19    207       INTERLEUKIN-6.
FT   DISULFID    65     71       POTENTIAL.
FT   DISULFID    94    104       POTENTIAL.
SQ   SEQUENCE   207 AA;  23770 MW;  F30D19F86AD6A600 CRC64;
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  Query Match           12.6%;  Score 199;  DB 1;  Length 207;
  Best Local Similarity  23.5%;  Pred. No. 3.43e-19;
  Matches    32;  Conservative   42;  Mismatches  58;  Indels   4;  Gaps   3;

Db      62 KELCKNDETCIKSHVAVSENNLNLPKMTEKDGCFQTGYNRDDCLVRITSGLLEFQVYLRY 121
           ::||     |     : :  :|:|| : : | |   |:|   || ::: |:::|:| :::
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     122 IRNKFQEGNNRDRAEHVQSSSKALI-EILKQEVKDPNKIVFPSPTANINLLAKLESQNDW 180
           :   |  |::    : ::  :|:|  :|  :|::   |  :::|  :  ||::|:: : |
Qy     111 LTTEF--GKSVINVDVMELLTKTLGWDI-QEELNKLTKTHYSPPKFDRGLLGRLQGLKYW 167

Db     181 QKVMTMQLILSNFEDF 196
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Qy     168 VRHFASFYVLSAMEKF 183


RESULT   14
ID   IL6_FELCA      STANDARD;      PRT;   208 AA.
AC   P41683;
DT   01-NOV-1995 (Rel. 32, Created)
DT   01-NOV-1995 (Rel. 32, Last sequence update)
DT   15-JUL-1998 (Rel. 36, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6.
OS   Felis silvestris catus (Cat).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Carnivora; Fissipedia; Felidae; Felis.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 94162386.
RA   Ohashi T., Matsumoto Y., Watari T., Goitsuka R., Tsujimoto H.,
RA   Hasegawa A.;
RT   "Molecular cloning of feline interleukin-6 cDNA.";
RL   J. Vet. Med. Sci. 55:941-944(1993).
RN   [2]
RP   SEQUENCE FROM N.A.
RC   TISSUE=LYMPHOCYTES;
RX   MEDLINE; 94052249.
RA   Bradley W.G., Gibbs C., Kraus L., Good R.A., Day N.K.;
RT   "Molecular cloning and characterization of a cDNA encoding feline
RT   interleukin-6.";
RL   Proc. Soc. Exp. Biol. Med. 204:301-305(1993).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC   ----------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; L16914; AAA16620.1; -.
DR   EMBL; D13227; BAA02507.1; -.
DR   HSSP; P05231; 2IL6.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Glycoprotein; Growth factor; Signal.
FT   SIGNAL        1     27       POTENTIAL.
FT   CHAIN        28    208       INTERLEUKIN-6.
FT   DISULFID     68     74       BY SIMILARITY.
FT   DISULFID     97    107       BY SIMILARITY.
FT   CONFLICT      2      2       T -> N (IN REF. 2).
FT   CONFLICT     45     45       S -> P (IN REF. 2).
FT   CONFLICT    133    133       E -> K (IN REF. 2).
FT   CONFLICT    173    187       AKLQSQEEWLRHTTI -> LSCSHRRVAEAHNN (IN
FT                                REF. 2).
FT   CONFLICT    200    201       FS -> LR (IN REF. 2).
SQ   SEQUENCE   208 AA;  23401 MW;  93B4456B2989CA4C CRC64;

  Query Match           12.0%;  Score 189;  DB 1;  Length 208;
  Best Local Similarity  25.6%;  Pred. No. 3.31e-17;
  Matches    34;  Conservative   31;  Mismatches  68;  Indels   0;  Gaps   0;

Db      65 KEMCDNYNKCEDSKEALAENNLNLPKLAEKDGCFQSGFNQETCLTRITTGLQEFQIYLKF 124
           :::|     |    |: |  :|:|| : : | |   |||: :|| ::: |: ||:: :||
Qy      51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db     125 LQDKYEGDEENAKSVYTSTNVLLQMLKRKGKNQDEVTIPVPTVEVGLQAKLQSQEEWLRH 184
           |   :    |  :   |: |  :    ::      : |  : || ::||:   |:||
Qy     111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db     185 TTIHLTLRRLEDF 197
           :    |  :|:|
Qy     171 FASFYVLSAMEKF 183


RESULT   15
ID   IL6_RAT        STANDARD;      PRT;   211 AA.
AC   P20607;
DT   01-FEB-1991 (Rel. 17, Created)
DT   01-FEB-1991 (Rel. 17, Last sequence update)
DT   15-JUL-1998 (Rel. 36, Last annotation update)
DE   INTERLEUKIN-6 PRECURSOR (IL-6).
GN   IL6 OR IL-6.
OS   Rattus norvegicus (Rat).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 89380206.
RA   Northemann W., Braciak T.A., Hattori M., Lee F., Fey G.H.;
RT   "Structure of the rat interleukin 6 gene and its expression in
RT   macrophage-derived cells.";
RL   J. Biol. Chem. 264:16072-16082(1989).
CC   -!- FUNCTION: IL6 IS A CYTOKINE WITH A WIDE VARIETY OF BIOLOGICAL
CC       FUNCTIONS: IT PLAYS AN ESSENTIAL ROLE IN THE FINAL DIFFERENTIATION
CC       OF B-CELLS INTO IG-SECRETING CELLS, IT INDUCES MYELOMA AND
CC       PLASMACYTOMA GROWTH, IT INDUCES NERVE CELLS DIFFERENTIATION, IN
CC       HEPATOCYTES IT INDUCES ACUTE PHASE REACTANTS.
CC   -!- SIMILARITY: BELONGS TO THE IL-6 SUPERFAMILY.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; M26744; AAA77659.1; -.
DR   EMBL; M26745; AAA41430.1; -.
DR   PIR; A34247; A34247.
DR   HSSP; P05231; 1ALU.
DR   PFAM; PF00489; IL6; 1.
DR   PRINTS; PR00433; IL6GCSFMGF.
DR   PRINTS; PR00434; INTERLEUKIN6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
KW   Cytokine; Growth factor; Glycoprotein; Signal.
FT   SIGNAL        1     24       POTENTIAL.
FT   CHAIN        25    211       INTERLEUKIN-6.
FT   DISULFID     70     76       BY SIMILARITY.
FT   DISULFID     99    109       BY SIMILARITY.
SQ   SEQUENCE   211 AA;  24357 MW;  17D248A14F96B5C1 CRC64;

  Query Match           12.0%;  Score 189;  DB 1;  Length 211;
  Best Local Similarity  25.7%;  Pred. No. 3.31e-17;
  Matches    39;  Conservative   40;  Mismatches  72;  Indels   1;  Gaps   1;
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Db      55 ITYVLREILEMRKELCNGNSDCMNSDDALSENNLKLPEIQRNDGCFQTGYNQEICLLKIC 114
           :  :|: | |  ::||   : |:   :: :  :|||| |   | |   |:|:  || |:
Qy      39 LNWMLWVIDECFRDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLA 98

Db     115 SGLLEFRFYLEFVKNNLQDNKKDKARVIQSNTETLVHIFKQEIKDSYKIVLPTPTSNALL 174
            |::||   : |:  ::  :  :   |::  | ||   : :|::   |   : |  :  |
Qy      99 DGFFEFEVLFKFLTTEFGKSVINVD-VMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGL 157

Db     175 MEKLESQKEWLRTKTIQLILKALEEFLKVTMR 206
           : :|:: | |:|  :   :| |:| |   ::|
Qy     158 LGRLQGLKYWVRHFASFYVLSAMEKFAGQAVR 189
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Search completed: Fri Sep 15 16:33:31 2000
Job time : 20 secs.

MPsrch_pp protein - protein database search, using Smith-Waterman algorithm

Run on: Fri Sep 15 16:33:48 2000; MasPar time 21.30 Seconds
664.171 Million cell updates/sec

Tabular output not generated.

Title: >US-09-230-048-2
Description: (1-204) from US09230048.pep
Perfect Score: 1579
Sequence: 1 MCWFKLWSLLLVGSLLVSGT.....GQAVRVLDSIPDVTPDVHDK 204

Scoring table: PAM 150
Gap 11

Searched: 225878 seqs, 69334122 residues

Post-processing: Minimum Match 0%
Listing first 45 summaries

Database: sptrembl12
1:sp_archea 2:sp_bacteria 3:sp_fungi 4:sp_human
5:sp_invertebrate 6:sp_mammal 7:sp_mhc 8:sp_organelle
9:sp_phage 10:sp_plant 11:sp_rodent 12:sp_unclassified
13:sp_vertebrate 14:sp_virus

Statistics: Mean 45.007; Variance 85.016; scale 0.529

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description	Pred. No.
1	1579	100.0	204	14	Q98823	INTERLEUKIN-6 HOMOLOG	0.00e+00
2	1573	99.6	204	14	O40918	ORF K2.	0.00e+00
3	252	16.0	209	6	O97540	INTERLEUKIN-6 (FRAGMEN	6.79e-27
4	227	14.4	208	6	Q9XT80	INTERLEUKIN 6 PRECURSO	3.58e-22
5	226	14.3	205	6	Q28747	INTERLEUKIN 6 (FRAGMEN	5.50e-22
6	201	12.7	209	6	Q28819	INTERLEUKIN 6 (FRAGMEN	2.18e-17
7	189	12.0	160	6	O97535	INTERLEUKIN-6 (FRAGMEN	3.12e-15
8	169	10.7	207	6	Q28403	INTERLEUKIN 6 (FRAGMEN	9.98e-12
9	169	10.7	210	11	Q9WVQ8	IL-6 (FRAGMENT).	9.98e-12
10	121	7.7	101	11	O55041	INTERLEUKIN 6 (FRAGMEN	6.07e-04
11	113	7.2	377	8	O46980	RIBULOSE BISPHOSPHATE	9.13e-03
12	111	7.0	669	3	O60021	VERY LONG-CHAIN FATTY	1.77e-02
13	109	6.9	421	14	O72903	FPI7L, ORTHOLOGUE OF V	3.40e-02
14	108	6.8	281	2	O67318	HYPOTHETICAL 32.6 KD P	4.71e-02
15	107	6.8	382	2	O85187	SODIUM-PROTON ANTIPORT	6.50e-02
16	108	6.8	737	11	O88478	PROSPERO-RELATED HOMEO	4.71e-02
17	106	6.7	515	14	Q98217	MC049L.	8.96e-02
18	105	6.6	131	13	O93356	PROX1 (FRAGMENT).	1.23e-01
19	104	6.6	197	1	Q58869	HYPOTHETICAL PROTEIN M	1.69e-01
20	104	6.6	628	4	O95052	BRG-1-HUMAN (FRAGMENT	1.69e-01
21	105	6.6	659	3	O59729	HYPOTHETICAL 74.1 KD P	1.23e-01
22	104	6.6	921	10	O04641	SIMILAR TO KINESIN.	1.69e-01
23	104	6.6	1022	11	Q63928	BRAHMA RELATED PROTEIN	1.69e-01
24	104	6.6	1630	13	Q90753	BRG1 PROTEIN.	1.69e-01
25	102	6.5	164	5	O44835	F54D12.1 PROTEIN.	3.17e-01
26	103	6.5	371	13	O93283	GAG POLYPROTEIN.	2.32e-01
27	102	6.5	428	2	Q9Z975	ATPASE.	3.17e-01
28	103	6.5	739	13	Q9YHZ4	HOMEODOMAIN PROTEIN.	2.32e-01
29	103	6.5	1568	13	Q90755	BRM PROTEIN.	2.32e-01
30	101	6.4	311	8	O98856	MATURASE (FRAGMENT).	4.33e-01
31	101	6.4	376	8	O46965	RIBULOSE BISPHOSPHATE	4.33e-01
32	101	6.4	377	8	O46964	RIBULOSE-1,5-BISPHOSPH	4.33e-01
33	100	6.3	305	5	Q20840	D-BETA-HYDROXYBUTYRATE	5.90e-01
34	97	6.1	515	3	O74626	ALK8 PROTEIN.	1.47e+00
35	96	6.1	516	5	O61577	KATANIN P60 SUBUNIT.	1.99e+00
36	96	6.1	1810	5	O44930	PUTATIVE VOLTAGE-GATED	1.99e+00
37	94	6.0	207	2	O25367	PHOSPHOSERINE PHOSPHAT	3.60e+00
38	95	6.0	423	14	Q89205	ORF6L.	2.68e+00
39	94	6.0	453	10	O80909	T19C21.9 PROTEIN.	3.60e+00
40	95	6.0	799	10	Q9XI39	F9L1.24 PROTEIN.	2.68e+00
41	94	6.0	2708	5	O15791	CHLOROQUINE RESISTANCE	3.60e+00
42	94	6.0	2742	5	O15801	CHLOROQUINE RESISTANCE	3.60e+00
43	94	6.0	2819	5	O15792	STRAIN HB3 CG2 (CG2).	3.60e+00
44	93	5.9	683	5	Q9Y136	BCDNA.GH07188.	4.83e+00
45	93	5.9	928	5	Q18696	C47G2.5 PROTEIN.	4.83e+00

ALIGNMENTS

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RESULT    1
ID   Q98823      PRELIMINARY;      PRT;   204 AA.
AC   Q98823;
DT   01-FEB-1997 (TrEMBLrel. 02, Created)
DT   01-FEB-1997 (TrEMBLrel. 02, Last sequence update)
DT   01-NOV-1998 (TrEMBLrel. 08, Last annotation update)
DE   INTERLEUKIN-6 HOMOLOG (FRAGMENT).
GN   VIL-6.
OS   Kaposi's sarcoma-associated herpesvirus (KSHV) (Human herpesvirus 8),
OS   and Kaposi's sarcoma-associated herpesvirus (KSHV)
OS   (Human herpesvirus 8).
OC   Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
OC   Gammaherpesvirinae; Rhadinovirus.
RN   [1]
RP   SEQUENCE FROM N.A.
RA   NEIPEL F., ALBRECHT J.C., ENSSER A., HUANG Y.Q., LI J.J.,
RA   FRIEDMAN-KIEN A.E., FLECKENSTEIN B.;
RL   Submitted (NOV-1996) to the EMBL/GenBank/DDBJ databases.
RN   [2]
RP   SEQUENCE FROM N.A.
RA   NICHOLAS J., RUVOLO V.R., BURNS W.H., SANDFORD G., WAN X., CIUFO D.,
RA   HENDRICKSON S., GUO H.G., HAYWARD G.S., REITZ M.S.;
RL   Submitted (SEP-1996) to the EMBL/GenBank/DDBJ databases.
RN   [3]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 97094384.
RA   MOORE P.S., BASHOFF C., WEISS R.A., CHANG Y.;
RT   "Molecular mimicry of human cytokine and cytokine response pathway
RT   genes by KSHV.";
RL   Science 274:1739-1744(1996).
RN   [4]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 97121480.
RA   RUSSO J.J., BOHENZKY R.A., CHIEN M.C., CHEN J., YAN M., MADDALENA D.,
RA   PARRY J.P., PERUZZI D., EDELMAN I.S., CHANG Y., MOORE P.S.;
RT   "Nucleotide sequence of the Kaposi sarcoma-associated herpesvirus
RT   (HHV8).";
RL   Proc. Natl. Acad. Sci. U.S.A. 93:14862-14867(1996).
RN   [5]
RP   SEQUENCE FROM N.A.
RA   RUSSO J.J., BOHENZKY R.A., CHIEN M.C., CHEN J., YAN M., MADDALENA D.,
RA   PARRY J.P., PERUZZI D., EDELMAN I.S., CHANG Y., MOORE P.S.;
RL   Submitted (OCT-1996) to the EMBL/GenBank/DDBJ databases.
RN   [6]
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RP   SEQUENCE FROM N.A.
RA   RUSSO J.J., BOHENZKY R.A., CHIEN M.C., CHEN J., YAN M., MADDALENA D.,
RA   PARRY J.P., PERUZZI D., EDELMAN I.S., CHANG Y., MOORE P.S.;
RL   Submitted (MAY-1997) to the EMBL/GenBank/DDBJ databases.
RN   [7]
RP   SEQUENCE FROM N.A.
RC   SPECIES=KSHV;
RA   SUN R., LIN S.-F., MILLER G.;
RL   Submitted (SEP-1996) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; U73655; AAB18244.1; -.
DR   EMBL; U67774; AAB61701.1; -.
DR   EMBL; U75698; AAC57089.1; -.
DR   EMBL; U71365; AAC34937.1; -.
DR   PFAM; PF00489; IL-6; 1.
FT   NON_TER     204    204
SQ   SEQUENCE   204 AA;  23408 MW;  77E3B980 CRC32;

  Query Match          100.0%;  Score 1579;  DB 14;  Length 204;
  Best Local Similarity 100.0%;  Pred. No. 0.00e+00;
  Matches   204;  Conservative    0;  Mismatches   0;  Indels   0;  Gaps   0;

Db      1 MCWFKLWSLLLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60
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Qy      1 MCWFKLWSLLLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60

Db     61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy     61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120

Db    121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy    121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180

Db    181 EKFAGQAVRVLDSIPDVTPDVHDK 204
          ||||||||||||||||||||||||
Qy    181 EKFAGQAVRVLDSIPDVTPDVHDK 204


RESULT    2
ID   O40918      PRELIMINARY;      PRT;   204 AA.
AC   O40918;
DT   01-JAN-1998 (TrEMBLrel. 05, Created)
DT   01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
DT   01-NOV-1998 (TrEMBLrel. 08, Last annotation update)
DE   ORF K2.
OS   Kaposi's sarcoma-associated herpesvirus (KSHV) (Human herpesvirus 8).
OC   Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
OC   Gammaherpesvirinae; Rhadinovirus.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 97138401.
RA   NEIPEL F., ALBRECHT J.C., ENSSER A., HUANG Y.Q., LI J.J.,
RA   FRIEDMAN-KIEN A.E., FLECKENSTEIN B.;
RT   "Human herpesvirus 8 encodes a homolog of interleukin-6.";
RL   J. Virol. 71:839-842(1997).
RN   [2]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 97296220.
RA   NEIPEL F., ALBRECHT J.C., FLECKENSTEIN B.;
RT   "Cell-homologous genes in the Kaposi's sarcoma-associated rhadinovirus
RT   human herpesvirus 8: determinants of its pathogenicity?";
RL   J. Virol. 71:4187-4192(1997).
DR   EMBL; U93872; AAB62676.1; -.
DR   PFAM; PF00489; IL-6; 1.
SQ   SEQUENCE   204 AA;  23408 MW;  54BB7A6F CRC32;

  Query Match          99.6%;  Score 1573;  DB 14;  Length 204;
  Best Local Similarity 99.5%;  Pred. No. 0.00e+00;
  Matches   203;  Conservative    1;  Mismatches   0;  Indels   0;  Gaps   0;

Db      1 MCWFKLWSILLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60
          ||||||||:||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy      1 MCWFKLWSLLLVGSLLVSGTRGKLPDAPEFEKDLLIQRLNWMLWVIDECFRDLCYRTGIC 60

Db     61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy     61 KGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVI 120

Db    121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy    121 NVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAM 180

Db    181 EKFAGQAVRVLDSIPDVTPDVHDK 204
          ||||||||||||||||||||||||
Qy    181 EKFAGQAVRVLDSIPDVTPDVHDK 204


RESULT    3
ID   O97540      PRELIMINARY;      PRT;   209 AA.
AC   O97540;
DT   01-MAY-1999 (TrEMBLrel. 10, Created)
DT   01-MAY-1999 (TrEMBLrel. 10, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   INTERLEUKIN-6 (FRAGMENT).
GN   IL-6.
OS   Aotus nancymaae (Owl monkey).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
OC   Eutheria; Primates; Platyrrhini; Cebidae; Aotinae; Aotus.
RN   [1]
RP   SEQUENCE FROM N.A.
RA   ECHEVERRY S.J., HERNANDEZ E., MORENO A., PATARROYO M.E., MURILLO L.A.;
RT   "Identification, cloning and sequencing of different interleukin genes
RT   in 4 Aotus species.";
RL   Submitted (JUL-1997) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF014510; AAD01536.1; -.
DR   HSSP; P05231; 1ALU.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
FT   NON_TER       1      1
FT   NON_TER     209    209
SQ   SEQUENCE   209 AA;  23406 MW;  99D77053 CRC32;

  Query Match          16.0%;  Score 252;  DB 6;  Length 209;
  Best Local Similarity 27.7%;  Pred. No. 6.79e-27;
  Matches    39;  Conservative   37;  Mismatches   65;  Indels   0;  Gaps   0;

Db     69 KETCNKSNMCESSKEALAENNLNLPKMAEKDGCFQSGFNEETCLVKIITGLLEFEVYLEY 128
          :: | :: :| :  |: |  :|:|| : : | |  |||| :|| |:  |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    129 LQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTNASLLTKLQAQNQWLQD 188
          |   |  |      ::: || |   :|   ::|     : |  : :|| :||: : |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    189 MTTHLILRSFKEFLQSSLRAL 209
          ::  :| :   |   ::| |
Qy    171 FASFYVLSAMEKFAGQAVRVL 191


RESULT    4
ID   Q9XT80      PRELIMINARY;      PRT;   208 AA.
AC   Q9XT80;
DT   01-NOV-1999 (TrEMBLrel. 12, Created)
DT   01-NOV-1999 (TrEMBLrel. 12, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   INTERLEUKIN 6 PRECURSOR.
OS   Delphinapterus leucas (Beluga whale).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
OC   Eutheria; Cetartiodactyla; Cetacea; Odontoceti; Monodontidae;
OC   Delphinapterus.
RN   [1]
RP   SEQUENCE FROM N.A.
RA   ST-LAURENT G., DE GUISE S., FOURNIER M., ARCHAMBAULT D.;
RT   "Molecular cloning and phylogenetic analysis of beluga whale
RT   (Delphinapterus leucas) interleukin 6.";
RL   Submitted (JUL-1998) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF076643; AAD42929.1; -.
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DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
SQ   SEQUENCE   208 AA;  23456 MW;  0FA70646 CRC32;

  Query Match           14.4%;  Score 227;  DB 6;  Length 208;
  Best Local Similarity  21.6%;  Pred. No. 3.58e-22;
  Matches   29;  Conservative   50;  Mismatches  54;  Indels   1;  Gaps   1;

Db     64 KEMCEKYDKCENSKEALAENNLNLPKMAEKDGCFQSGFNQETCLMRITTGLLEYQIYLDY 123
           :::| :   |    |: |  :|:|| : : | |   |||: :||:::: |::|::: : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    124 LQNEYEGDKGSIEAVQISIKALAQILRQKVKNPDEVTTPDPTTNASLMNNLQSQNDDWMR 183
           |  |:     ::: :::  |:|:  ::: :::      : |  : :|:  ||: :  |:|
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKY-WVR 169

Db    184 NTKIILILRSLENF 197
          :   : :| ::|:|
Qy    170 HFASFYVLSAMEKF 183


RESULT    5
ID   Q28747      PRELIMINARY;      PRT;   205 AA.
AC   Q28747;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   INTERLEUKIN 6 (FRAGMENT).
GN   IL-6.
OS   Orcinus orca (Killer whale).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
OC   Eutheria; Cetartiodactyla; Cetacea; Odontoceti; Delphinidae; Orcinus.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 96163018.
RA   KING D.P., SCHRENZEL M.D., MCKNIGHT M.L., REIDARSON T.H., HANNI K.D.,
RA   STOTT J.L., FERRICK D.A.;
RT   "Molecular cloning and sequencing of interleukin 6 cDNA fragments from
RT   the harbor seal (Phoca vitulina), killer whale (Orcinus orca), and
RT   Southern sea otter (Enhydra lutris nereis).";
RL   Immunogenetics 43:190-195(1996).
DR   EMBL; L46803; AAB01429.1; -.
DR   HSSP; P05231; 1ALU.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
DR   PFAM; PF00489; IL-6; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   205 AA;  23266 MW;  C853C8DF CRC32;

  Query Match           14.3%;  Score 226;  DB 6;  Length 205;
  Best Local Similarity  20.4%;  Pred. No. 5.50e-22;
  Matches   29;  Conservative   54;  Mismatches  58;  Indels   1;  Gaps   1;

Db     61 KEMCEKYDKCENSKEALAENNLNLPKMAEKDGCFQSGFNQETCLMRITTGLLEYQIYLDY 120
           :::| :   |    |: |  :|:|| : : | |   |||: :||:::: |::|::: : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    121 LQNEYEGDKEAIEAVQISSKALAQILRQKVKNPDEVTTPDPTTNASLMNNLQSQNDDWMK 180
           |  |:      :: ::: :|:|:  ::: :::      : |  : :|:  ||: :  |::
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKY-WVR 169

Db    181 NTKIILILRSLENFLQFSLRAI 202
          :   : :| ::|:|   ::| :
Qy    170 HFASFYVLSAMEKFAGQAVRVL 191


RESULT    6
ID   Q28819      PRELIMINARY;      PRT;   209 AA.
AC   Q28819;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   INTERLEUKIN 6 (FRAGMENT).
GN   IL-6.
OS   Phoca vitulina (Harbor seal).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
OC   Eutheria; Carnivora; Pinnipedia; Phocidae; Phoca.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 96163018.
RA   KING D.P., SCHRENZEL M.D., MCKNIGHT M.L., REIDARSON T.H., HANNI K.D.,
RA   STOTT J.L., FERRICK D.A.;
RT   "Molecular cloning and sequencing of interleukin 6 cDNA fragments from
RT   the harbor seal (Phoca vitulina), killer whale (Orcinus orca), and
RT   Southern sea otter (Enhydra lutris nereis).";
RL   Immunogenetics 43:190-195(1996).
DR   EMBL; L46802; AAB01430.1; -.
DR   HSSP; P05231; 2IL6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
DR   PFAM; PF00489; IL-6; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   209 AA;  23483 MW;  29B594E3 CRC32;

  Query Match           12.7%;  Score 201;  DB 6;  Length 209;
  Best Local Similarity  22.6%;  Pred. No. 2.18e-17;
  Matches   30;  Conservative   42;  Mismatches  61;  Indels   0;  Gaps   0;

Db     66 KEMCDKYNKCEDSKEALAENNLRLPKLAEKDGCFQSGFNQETCLTRITTGLLEFQIHLKY 125
           :::| :   |    |: |  :|:|| : : | |   |||: :|| ::: |::|:: :|:
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    126 IQANYEGNKEDANSVYISTKLLVQMLMKKVKSQDEVTTPDPTTDTSLQAILKAQDKWLKH 185
          : :::  :  : : : : || |   :   ::       : |  | :| : | :   |::|
Qy    111 LTTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRH 170

Db    186 TTIHLILRSLEDF 198
          :   :| ::| |
Qy    171 FASFYVLSAMEKF 183


RESULT    7
ID   O97535      PRELIMINARY;      PRT;   160 AA.
AC   O97535;
DT   01-MAY-1999 (TrEMBLrel. 10, Created)
DT   01-MAY-1999 (TrEMBLrel. 10, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   INTERLEUKIN-6 (FRAGMENT).
GN   IL-6.
OS   Aotus vociferans.
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
OC   Eutheria; Primates; Platyrrhini; Cebidae; Aotinae; Aotus.
RN   [1]
RP   SEQUENCE FROM N.A.
RA   ECHEVERRY S.J., HERNANDEZ E., MORENO A., PATARROYO M.E., MURILLO L.A.;
RT   "Identification, cloning and sequencing of different interleukin genes
RT   in 4 Aotus species.";
RL   Submitted (JUL-1997) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF014505; AAD01531.1; -.
DR   HSSP; P05231; 2IL6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   160 AA;  17855 MW;  EF6090C3 CRC32;

  Query Match           12.0%;  Score 189;  DB 6;  Length 160;
  Best Local Similarity  32.1%;  Pred. No. 3.12e-15;
  Matches   26;  Conservative   23;  Mismatches  32;  Indels   0;  Gaps   0;

Db     69 KEICDKSNMCESSKEALAENNLNLPKMAEKDGCFQSGFNEETCLLKITTGLLEFEVYLEY 128
           :::| :: :| :  |: |  :|:|| : : | |   |||| :|| |:: |::|||| : :
Qy     51 RDLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKF 110

Db    129 LQNRFESSKEQAGAVQMSTKA 149
          |   |  |      ::: ||:
Qy    111 LTTEFGKSVINVDVMELLTKT 131


RESULT    8
ID   Q28403      PRELIMINARY;      PRT;   207 AA.
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AC   Q28403;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   INTERLEUKIN 6 (FRAGMENT).
GN   IL-6.
OS   Enhydra lutris (Sea otter).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
OC   Eutheria; Carnivora; Fissipedia; Mustelidae; Enhydra.
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE; 96163018.
RA   KING D.P., SCHRENZEL M.D., MCKNIGHT M.L., REIDARSON T.H., HANNI K.D.,
RA   STOTT J.L., FERRICK D.A.;
RT   "Molecular cloning and sequencing of interleukin 6 cDNA fragments from
RT   the harbor seal (Phoca vitulina), killer whale (Orcinus orca), and
RT   Southern sea otter (Enhydra lutris nereis).";
RL   Immunogenetics 43:190-195(1996).
DR   EMBL; L46804; AAB01428.1; -.
DR   HSSP; P05231; 2IL6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
DR   PFAM; PF00489; IL-6; 1.
FT   NON_TER       1       1
SQ   SEQUENCE   207 AA;  23527 MW;  0F2CAC62 CRC32;

  Query Match           10.7%;  Score 169;  DB 6;  Length 207;
  Best Local Similarity  23.6%;  Pred. No. 9.98e-12;
  Matches   33;  Conservative   40;  Mismatches  65;  Indels   2;  Gaps   2;

Db     67 EMCDKYNKCEDSKEVLAENNLNLPKLAEKDRCFQSRFNQETCLTRITTGLQEFQIHLKYL 126
          ::| :   |    |  |  :|:|| : : |:|    ||: :|| ::: |: ||:: :|:|
Qy     52 DLCYRTGICKGILEPAAIFHLKLPAINDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFL 111

Db    127 ESNYEGNKDNAHSVYISTKHL-LQTLRPMNQIEVTT-PDPTTDASLQALFKSQDKWLKHT 184
          :::  :  |   : : || |  :    :| :  |  : |  | :| : : :   |::|
Qy    112 TTEFGKSVINVDVMELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHF 171

Db    185 TIHLILRRLEDFLQFSLRAI 204
          :   :|  :| |   ::| :
Qy    172 ASFYVLSAMEKFAGQAVRVL 191


RESULT    9
ID   Q9WVQ8      PRELIMINARY;      PRT;   210 AA.
AC   Q9WVQ8;
DT   01-NOV-1999 (TrEMBLrel. 12, Created)
DT   01-NOV-1999 (TrEMBLrel. 12, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   IL-6 (FRAGMENT).
OS   Mesocricetus auratus (Golden hamster).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
OC   Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae; Mesocricetus.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=APA; TISSUE=KIDNEY;
RA   NISHIDA E.;
RT   "APA hamsters IL-6 partial cDNA.";
RL   Submitted (JUN-1999) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AB028635; BAA78766.1; -.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
FT   NON_TER       1       1
SQ   SEQUENCE   210 AA;  24060 MW;  0307F113 CRC32;

  Query Match           10.7%;  Score 169;  DB 11;  Length 210;
  Best Local Similarity  24.0%;  Pred. No. 9.98e-12;
  Matches   40;  Conservative   41;  Mismatches  84;  Indels   2;  Gaps   2;

Db     39 PNRPVYTTSQQVGGLVTYVLREIYELRKELCNNNPGCMDNDYVLLENNLELPVIQINDGC 98
          |: | :     :  |   :|: | |  ::||     |:         :| || |   | |
Qy     25 PDAPEFEKDLLIQRL-NWMLWVIDECFRDLCYRTGICKGILEPAAIFHLKLPAINDTDHC 83

Db     99 LQTGYNWEICLLKITSGLLDYQIYLEFVTNNVQDNKKDKARVIQSTIKTLSQIFKQEVKG 158
             |:|   || |:: |:::::: : |:| :   :  :   |::   |||:  : :|::
Qy     84 GLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVINVD-VMELLTKTLGWDIQEELNK 142

Db    159 PDKIVTPSPTSKAILMEKLESQKEWPRTKTIKLILKALEEFLEVTMR 205
             |   ::|     |: :|:: | | |  :   :| |:| |   ::|
Qy    143 LTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAMEKFAGQAVR 189


RESULT   10
ID   O55041      PRELIMINARY;      PRT;   101 AA.
AC   O55041;
DT   01-JUN-1998 (TrEMBLrel. 06, Created)
DT   01-JUN-1998 (TrEMBLrel. 06, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   INTERLEUKIN 6 (FRAGMENT).
GN   IL-6.
OS   Cricetulus griseus (Chinese hamster).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
OC   Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae; Cricetulus.
RN   [1]
RP   SEQUENCE FROM N.A.
RA   HEINE H., DELUDE R.D., MONKS B., GOLENBOCK D.T.;
RL   Submitted (JAN-1998) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF044667; AAC02100.1; -.
DR   HSSP; P05231; 2IL6.
DR   PROSITE; PS00254; INTERLEUKIN_6; 1.
DR   PFAM; PF00489; IL-6; 1.
FT   NON_TER       1       1
FT   NON_TER     101     101
SQ   SEQUENCE   101 AA;  11749 MW;  D1DA362A CRC32;

  Query Match           7.7%;  Score 121;  DB 11;  Length 101;
  Best Local Similarity  25.5%;  Pred. No. 6.07e-04;
  Matches   24;  Conservative   27;  Mismatches  42;  Indels   1;  Gaps   1;

Db      2 IQRNDGCYQTGYNWEICLLKITSGLLDYQIYLEFVTNNVQDNKKDKARVIQSTTKTLSQI 61
            |   | |   |:|   || |:: |:::::: : |:| :   :  :   |::  ||||:
Qy     77 INDTDHCGLIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVINVD-VMELLTKTLGWD 135

Db     62 FKQEVKDPDKIVMPSPTSKAILIEKLESQKQWPR 95
          : :|::   |   ::|     |: :|:: | | |
Qy    136 IQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVR 169


RESULT   11
ID   O46980      PRELIMINARY;      PRT;   377 AA.
AC   O46980;
DT   01-JUN-1998 (TrEMBLrel. 06, Created)
DT   01-JUN-1998 (TrEMBLrel. 06, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   RIBULOSE BISPHOSPHATE CARBOXYLASE LARGE CHAIN (EC 4.1.1.39)
DE   (FRAGMENT).
GN   RBCL.
OS   Synura uvella.
OG   Chloroplast.
OC   Eukaryota; stramenopiles; Chrysophyceae; Synurales; Synura.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=CCMP870;
RA   DAUGBJERG N., ANDERSEN R.A.;
RL   J. Phycol. 33:1031-1041(1997).
CC   -!- FUNCTION: RUBISCO CATALYSES TWO REACTIONS: THE CARBOXYLATION OF D-
CC       RIBULOSE 1,5-BISPHOSPHATE, THE PRIMARY EVENT IN PHOTOSYNTHETIC
CC       CARBON DIOXIDE FIXATION, AS WELL AS THE OXIDATIVE FRAGMENTATION OF
CC       THE PENTOSE SUBSTRATE IN THE PHOTORESPIRATION PROCESS. BOTH
CC       REACTIONS OCCUR SIMULTANEOUSLY AND IN COMPETITION AT THE SAME
CC       ACTIVE SITE.
CC   -!- CATALYTIC ACTIVITY: D-RIBULOSE 1,5-BISPHOSPHATE + CO(2) = 2 3-
CC       PHOSPHO-D-GLYCERATE.
CC   -!- CATALYTIC ACTIVITY: D-RIBULOSE 1,5-BISPHOSPHATE + O(2) = 3-
CC       PHOSPHO-D-GLYCERATE + 2-PHOSPHOGLYCOLATE.
CC   -!- SUBUNIT: 8 LARGE CHAINS + 8 SMALL CHAINS.
DR   EMBL; AF015586; AAC02925.1; -.
DR   PROSITE; PS00157; RUBISCO_LARGE; 1.
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DR   PFAM; PF00016; RuBisCO_large; 1.
KW   Chloroplast; Photosynthesis; Carbon dioxide fixation;
KW   Photorespiration; Lyase; Oxidoreductase; Monooxygenase.
FT   NON_TER       1      1
FT   ACT_SITE    175    175       BINDING OF CO(2) ACTIVATES THE ENZYME.
FT   NON_TER     377    377
SQ   SEQUENCE   377 AA;  41860 MW;  84098E6D CRC32;

  Query Match             7.2%;  Score 113;  DB 8;  Length 377;
  Best Local Similarity  26.8%;  Pred. No. 9.13e-03;
  Matches    22;  Conservative   21;  Mismatches  34;  Indels   5;  Gaps   5;

Db     97 VFGFKAVKCLR-LEDMRLPYAYLKTFLGPATG-VIVERERMDVFGRPLLGATVKPKLG-L 153
          ::||:   ||: | |  : :  |  ||    |  ::: : |::: : | |  :   |  |
Qy     85 LIGFNETSCLKKLADGFFEFEVLFKFLTTEFGKSVINVDVMELLTKTL-GWDIQEELNKL 143

Db    154 SGKNYGRVVYE-GLKGGLDFLK 174
          :  :|:   :: || | |: ||
Qy    144 TKTHYSPPKFDRGLLGRLQGLK 165


RESULT   12
ID   O60021      PRELIMINARY;      PRT;   669 AA.
AC   O60021;
DT   01-AUG-1998 (TrEMBLrel. 07, Created)
DT   01-AUG-1998 (TrEMBLrel. 07, Last sequence update)
DT   01-NOV-1999 (TrEMBLrel. 12, Last annotation update)
DE   VERY LONG-CHAIN FATTY ACYL-COA SYNTHETASE.
GN   FAT1.
OS   Saccharomyces cerevisiae (Baker's yeast).
OC   Eukaryota; Fungi; Ascomycota; Hemiascomycetes; Saccharomycetales;
OC   Saccharomycetaceae; Saccharomyces.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=YPH680;
RA   WATKINS P.A., LU J.-F., STEINBERG S.J., GOULD S.J., SMITH K.D.,
RA   BRAITERMAN L.T.;
RL   J. Biol. Chem. 0:0-0(1998).
DR   EMBL; AF065148; AAC17118.1; -.
DR   PROSITE; PS00455; AMP_BINDING; 1.
DR   PFAM; PF00501; AMP-binding; 1.
SQ   SEQUENCE   669 AA;  77140 MW;  BD93FC3D CRC32;

  Query Match             7.0%;  Score 111;  DB 3;  Length 669;
  Best Local Similarity  23.0%;  Pred. No. 1.77e-02;
  Matches    20;  Conservative   27;  Mismatches  36;  Indels   4;  Gaps   4;

Db    575 KLTDNSLDITAKTKLLNDSLSRLNLPSYAMPLFVKFVD-EIKMTDNHKILKKVYREQKLP 633
          ||:|  :::    |:|   :::  :    | |: | :  :|   : :|: |  |   |:
Qy     96 KLADGFFEFEVLFKFLTTEFGKSVINVDVMELLTKTLGWDIQ-EELNKLTKTHYSPPKFD 154

Db    634 KGLDGN-DTI-FWLKNYKRYEVLTAAD 658
          :|| |  : : :|:::  : ||:| :
Qy    155 RGLLGRLQGLKYWVRHFASFYVLSAME 181


RESULT   13
ID   O72903      PRELIMINARY;      PRT;   421 AA.
AC   O72903;
DT   01-AUG-1998 (TrEMBLrel. 07, Created)
DT   01-AUG-1998 (TrEMBLrel. 07, Last sequence update)
DT   01-NOV-1998 (TrEMBLrel. 08, Last annotation update)
DE   FPI7L, ORTHOLOGUE OF VACCINIA I7L.
GN   FPI7L.
OS   Fowlpox virus.
OC   Viruses; dsDNA viruses, no RNA stage; Poxviridae; Chordopoxvirinae;
OC   Avipoxvirus.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=HP-440;
RA   POLLITT E., SKINNER M.A., HEAPHY S.;
RL   Submitted (JAN-1998) to the EMBL/GenBank/DDBJ databases.
RN   [2]
RP   SEQUENCE FROM N.A.
RC   STRAIN=HP-440;
RX   MEDLINE; 87316919.
RA   BINNS M.M., STENZLER L., TOMLEY F.M., CAMPBELL J., BOURSNELL M.E.G.;
RT   "Identification by a random sequencing strategy of the fowlpoxvirus
RT   DNA polymerase gene, its nucleotide sequence and comparison with other
RT   viral DNA polymerases.";
RL   Nucleic Acids Res. 15:6563-6573(1987).
RN   [3]
RP   SEQUENCE FROM N.A.
RC   STRAIN=HP-440;
RX   MEDLINE; 92410746.
RA   BINNS M.M., BOURSNELL M.E.G., SKINNER M.A.;
RT   "Gene translocations in poxviruses: the fowlpox virus thymidine kinase
RT   gene is flanked by 15 bp direct repeats and occupies the locus which
RT   in vaccinia virus is occupied by the ribonucleotide reductase large
RT   subunit gene.";
RL   Virus Res. 24:161-172(1992).
DR   EMBL; AJ223385; CAA11298.1; -.
SQ   SEQUENCE   421 AA;  48621 MW;  8A6C19AB CRC32;

  Query Match             6.9%;  Score 109;  DB 14;  Length 421;
  Best Local Similarity  36.4%;  Pred. No. 3.40e-02;
  Matches    16;  Conservative   13;  Mismatches  13;  Indels   2;  Gaps   2;

Db    282 GLNRNSYLSSLANENADIDILFNFFIDNYGVTAGCINVEVNQLL 325
          |:|  | |  ||:   ::::||:|:  ::|  :  |||:| :||
Qy     87 GFNETSCLKKLADGFFEFEVLFKFLTTEFG-KSV-INVDVMELL 128


RESULT   14
ID   O67318      PRELIMINARY;      PRT;   281 AA.
AC   O67318;
DT   01-AUG-1998 (TrEMBLrel. 07, Created)
DT   01-AUG-1998 (TrEMBLrel. 07, Last sequence update)
DT   01-NOV-1998 (TrEMBLrel. 08, Last annotation update)
DE   HYPOTHETICAL 32.6 KD PROTEIN.
GN   AQ_1286.
OS   Aquifex aeolicus.
OC   Bacteria; Aquificales; Aquificaceae; Aquifex.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=VF5;
RX   MEDLINE; 98196666.
RA   DECKERT G., WARREN P.V., GAASTERLAND T., YOUNG W.G., LENOX A.L.,
RA   GRAHAM D.E., OVERBEEK R., SNEAD M.A., KELLER M., AUJAY M., HUBER R.,
RA   FELDMAN R.A., SHORT J.M., OLSON G.J., SWANSON R.V.;
RT   "The complete genome of the hyperthermophilic bacterium Aquifex
RT   aeolicus.";
RL   Nature 392:353-358(1998).
RN   [2]
RP   SEQUENCE FROM N.A.
RC   STRAIN=VF5;
RA   DECKERT G., WARREN P.V., GAASTERLAND T., YOUNG W.G., LENOX A.L.,
RA   GRAHAM D.E., OVERBEEK R., SNEAD M.A., KELLER M., AUJAY M., HUBER R.,
RA   FELDMAN R.A., SHORT J.M., OLSON G.J., SWANSON R.V.;
RL   Submitted (JUL-1997) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AE000732; AAC07279.1; -.
KW   Hypothetical protein.
SQ   SEQUENCE   281 AA;  32624 MW;  233502A9 CRC32;

  Query Match             6.8%;  Score 108;  DB 2;  Length 281;
  Best Local Similarity  35.9%;  Pred. No. 4.71e-02;
  Matches    23;  Conservative   14;  Mismatches  20;  Indels   7;  Gaps   7;

Db    170 EGLFEFLTV-FSKGKVNINTAPLLVLYSLDRDIDMELAKRI-ADYRKEKPFKQLKDLL-M 226
          | || |||  |:|: :|::   ||   :| :||: || |   : |   | | : : ||
Qy    105 EVLFKFLTTEFGKSVINVDVMELLTK-TLGWDIQEELNKLTKTHYSPPK-F-D-RGLLGR 160

Db    227 VEGM 230
          ::|:
Qy    161 LQGL 164
```

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RESULT   15
ID   O85187      PRELIMINARY;      PRT;   382 AA.
AC   O85187;
DT   01-NOV-1998 (TrEMBLrel. 08, Created)
DT   01-NOV-1998 (TrEMBLrel. 08, Last sequence update)
DT   01-NOV-1998 (TrEMBLrel. 08, Last annotation update)
DE   SODIUM-PROTON ANTIPORTER AFFECTING PROTEIN.
GN   NHAA.
OS   Vibrio cholerae.
OC   Bacteria; Proteobacteria; gamma subdivision; Vibrionaceae; Vibrio.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=01 PERU 91;
RA   VIMONT S.J., BERCHE P.;
RT   "Isolation and molecular characterization of Vibrio cholerae nhaA
RT   gene.";
RL   Submitted (FEB-1998) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF051158; AAC33562.1; -.
SQ   SEQUENCE   382 AA;  40316 MW;  817BD6C5 CRC32;

  Query Match           6.8%;  Score 107;  DB 2;  Length 382;
  Best Local Similarity  22.3%;  Pred. No. 6.50e-02;
  Matches    29;  Conservative   31;  Mismatches  65;  Indels   5;  Gaps   5;

Db    146 VFLLALAIIDDLGVVVIIALFYSSDLSTIALTIGFIMTGVLFMLNAKHVTKLSIYLVAGL 205
          :| | |: |:|     :|: |  :       |: ||:   |||:: :    | |:  |  :
Qy     69 IFHLKLPAINDTDHCGLIG-FNETS-CLKKLADGFFEFEVLFKFLTTEFGK-SVINVDVM 125

Db    206 ILWIAVLKSGVHATLAGVVIGFAIPLKGNKGEHSPLKHLEHALHPYVAFAILPVFA-FAN 264
          |   |   ::  |  :      | | ::|  : |  |   :: : :| :|:    ||
Qy    126 ELLTKTLGWDIQEELNKLTKTHYSPPKFDRGLLGRLQGLKYWVRHFASFYVLSAMEKFAG 185

Db    265 AGIS-LQGVS 273
          ::  |::::
Qy    186 QAVRVLDSIP 195


Search completed: Fri Sep 15 16:34:15 2000
Job time : 27 secs.
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**********STN Columbus **********
**

FILE 'HOME' ENTERED AT 16:30:20 ON 15 SEP 2000

=> file medline

COST IN U.S. DOLLARS                SINCE FILE    TOTAL
                                    ENTRY SESSION
FULL ESTIMATED COST                      0.15     0.15

FILE 'MEDLINE' ENTERED AT 16:30:25 ON 15 SEP 2000

 FILE LAST UPDATED: 7 SEP 2000 (20000907/UP). FILE
COVERS 1960 TO DATE.

 MEDLINE has been reloaded to reflect the annual MeSH changes
made by
 the National Library of Medicine for 2000. Enter HELP RLOAD for
details.

 The OLDMEDLINE file segment now contains data from 1958
through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in
the
 Basic Index.  See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY
AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> s herpes virus type 8/ab,bi

      33818 HERPES/BI
     294323 VIRUS/BI
     529956 TYPE/BI
     749460 8/BI
    5408175 AB/FA
          9 HERPES VIRUS TYPE 8/AB
            ((HERPES(W)VIRUS(W)TYPE(W)8)/BI (L) AB/FA)
      33818 HERPES/BI
     294323 VIRUS/BI
     529956 TYPE/BI
     749460 8/BI
         14 HERPES VIRUS TYPE 8/BI
            ((HERPES(W)VIRUS(W)TYPE(W)8)/BI)
L1        14 HERPES VIRUS TYPE 8/AB,BI

=> s l1 and interleukin#/ab,bi

      90758 INTERLEUKIN#/BI
    5408175 AB/FA
      59796 INTERLEUKIN#/AB
            (INTERLEUKIN#/BI (L) AB/FA)
      90758 INTERLEUKIN#/BI
L2        1 L1 AND INTERLEUKIN#/AB,BI

=> d bib ab

L2  ANSWER 1 OF 1  MEDLINE
AN  97054369    MEDLINE
DN  97054369
TI  The natural history and molecular heterogeneity of HIV-associated
primary
    malignant lymphomatous effusions.
AU  Komanduri K V; Luce J A; McGrath M S; Herndier B G; Ng V
L
CS  Department of Medicine, University of California, San Francisco,
USA.
NC  RO1 CA54742 (NCI)
SO  JOURNAL OF ACQUIRED IMMUNE DEFICIENCY
SYNDROMES AND HUMAN RETROVIROLOGY,
    (1996 Nov 1) 13 (3) 215-26.
    Journal code: B7J. ISSN: 1077-9450.
CY  United States
DT  Journal; Article; (JOURNAL ARTICLE)
LA  English
FS  Priority Journals
EM  199702
AB  Primary malignant lymphomatous effusions arising in individuals
infected
    with the human immunodeficiency virus, type 1 (HIV-1) represent
a rare
    subset of HIV-associated lymphomas. Previous studies have
demonstrated
    that the malignant cells are monoclonal (as defined by
rearrangement of
    the immunoglobulin gene), express cell surface CD38, and are
infected with
    Epstein-Barr virus (EBV) and human  ***herpes***
***virus*** ,
     ***type***  ***8***  (HHV-8). Despite these detailed
molecular and
    immunophenotypic studies, clinical information on this disease
entity is
    scant, prompting us to review the clinical features of eight cases
seen at
    our institutions. All eight patients had total peripheral CD4+
lymphocytes
    < 200/microliter and presented with complaints related to body
cavity
    distension. Routine laboratory values were nondiagnostic and
yielded no
    prognostic information. Only two patients could tolerate and thus
received
    chemotherapy with no obvious impact on their clinical course. The
mean
    overall survival after diagnosis was 60 days (range 6-166 days).
Four
    patients were examined at autopsy. The primary malignant
lymphomatous
    effusion either was the immediate cause of death or contributed
    significantly to the death of only two. All four patients examined
post
    mortem, however, had lymphomatous infiltration of serosal
surfaces
    adjacent to the site of the primary malignant effusion. Molecular
and
    immunologic studies performed on the malignant cells and effusion
fluids
    revealed universal expression of cell surface CD38 and the
presence of
    HHV-8 gene sequences, but in contrast with previous studies, only
four had
    rearranged immunoglobulin genes or EBV present: IL-6 and IL-10
levels in
    the malignant effusion fluids were markedly elevated. In summary,
this
    rare subset of HIV-associated lymphomas in our eight patients
arose late
    in the course of HIV-associated disease, had a rapid clinical course,
and
    was molecularly heterogeneous. A pathogenetic role for HHV-8
alone in this
    disease process is strengthened by our observation of four cases
lacking
    EBV but containing HHV-8.

=> s hhv-8/ab,bi

       1308 HHV/BI
     749460 8/BI
    5408175 AB/FA
        396 HHV-8/AB
            ((HHV(W)8)/BI (L) AB/FA)
       1308 HHV/BI
     749460 8/BI
        458 HHV-8/BI
            ((HHV(W)8)/BI)
L3      458 HHV-8/AB,BI

=> s l3 and interleukin##/ab,bi

      90769 INTERLEUKIN##/BI
    5408175 AB/FA
      59812 INTERLEUKIN##/AB
            (INTERLEUKIN##/BI (L) AB/FA)
      90769 INTERLEUKIN##/BI
L4       38 L3 AND INTERLEUKIN##/AB,BI

=> s l4 and il-6/ab,bi

      87055 IL/BI
    1135699 6/BI
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5408175 AB/FA
14922 IL-6/AB
((IL(W)6)/BI (L) AB/FA)
87055 IL/BI
1135699 6/BI
15169 IL-6/BI
((IL(W)6)/BI)
L5 16 L4 AND IL-6/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 16 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 16 MEDLINE
AN 2000405417 MEDLINE
DN 20321451
TI Human herpesvirus 8-encoded ***interleukin*** -6 homologue (viral
IL - ***6***) induces endogenous human ***IL*** - ***6***
secretion.
AU Mori Y; Nishimoto N; Ohno M; Inagi R; Dhepakson P; Amou K; Yoshizaki K;
Yamanishi K
CS Department of Microbiology, Osaka University Medical School, Osaka
University Medical School, Osaka University, Osaka, Japan..
ymori@micro.med.osaka-u.ac.jp
SO JOURNAL OF MEDICAL VIROLOGY, (2000 Jul) 61 (3) 332-5.
Journal code: I9N. ISSN: 0146-6615.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200010
EW 20001004
AB We found that human herpesvirus 8-encoded ***IL*** - ***6*** (vIL-6)
induced endogenous human ***IL*** - ***6*** (huIL-6) secretion from
various cell lines (MT-4, THP-1, U937, Raji, and CESS) including patients
with multicentric Castleman's disease. Especially, in MT-4 cells, huIL-6
was enhanced with vIL-6 by 30-fold compared with that of control. In
addition, reverse transcriptase-polymerase chain reaction confirmed that
vIL-6 induced huIL-6 expression in MT-4 cells. Our novel finding of the
huIL-6 induction by vIL-6 indicates that vIL-6 may play a significant role
in the pathogenesis of ***HHV*** - ***8*** associated diseases.
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L5 ANSWER 2 OF 16 MEDLINE
AN 2000363450 MEDLINE
DN 20363450
TI Presence of human herpesvirus-8 DNA sequences and overexpression of human
IL - ***6*** and cyclin D1 in inflammatory myofibroblastic tumor
(inflammatory pseudotumor).
AU Gomez-Roman J J; Ocejo-Vinyals G; Sanchez-Velasco P; Nieto E H;
Leyva-Cobian F; Val-Bernal J F
CS Departamento de Anatomia Patologica, Hospital Universitario Marques de
Valdecilla, Instituto Nacional de la Salud, Facultad de Medicina,
Universidad de Cantabria, Santander, Spain.
SO LABORATORY INVESTIGATION, (2000 Jul) 80 (7) 1121-6.
Journal code: KZ4. ISSN: 0023-6837.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 200010
EW 20001001
AB Inflammatory myofibroblastic tumor (IMT) is composed of myofibroblasts,
plasma cells, and lymphocytes. Cytokines are possibly involved in its
pathogenesis. Human herpesvirus-8 (***HHV*** - ***8***) encodes cell
cycle regulatory and signaling proteins. A combination of nested PCR with
several negative controls and Southern blot methods showed the presence of
HHV - ***8*** DNA in seven cases of IMT. Additionally, strong
expression was demonstrated by in situ hybridization in many tumoral
nuclei. Most of the myofibroblasts in all of the cases were immunoreactive
for human ***IL*** - ***6*** and cyclin D1. These cytokines probably
have a paracrine action and may sustain myofibroblastic growth.
HHV - ***8*** could play an essential role in triggering IMT
development by a local reactivation of viral lytic replication. The
relationship between ***HHV*** - ***8*** and immunosuppression
status as the only associated cause for tumorigenesis should be revised.

L5 ANSWER 3 OF 16 MEDLINE
AN 2000122659 MEDLINE
DN 20122659
TI Castleman's disease.
AU Palestro G; Turrini F; Pagano M; Chiusa L
CS Departement of Biomedical Science and Human Oncology, University of
Torino, Torino, I-10126, Italy.. palestro@molinette.unito.it
SO Adv Clin Path, (1999 Jan-Apr) 3 (1-2) 11-22. Ref: 60
Journal code: DD0. ISSN: 1125-5552.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200004
EW 20000403
AB Castleman's disease (CD) is a rare atypical lymphoproliferative disorder
whose morphology, soon after the original presentation of Castleman et
al., has been definitely subdivided in a hyaline vascular (HV) and plasma
cell (PC) histopathological pattern, with intermediate variants. The
former occurs much more frequently than the latter and is usually
localized to the mediastinum or pulmonary hilum. The latter involves lymph
nodes separately or in aggregations and often displays multicentricity
with systemic symptoms including autoimmune phenomena and aggressive
course. Infections are the most frequent causes of patient demise in these
cases, followed by malignancies such as Kaposi's sarcoma, malignant
lymphoma or epithelial neoplasia. Increase of follicular dendritic
reticulum cells (FDRC), often dysplastic, in the germinal center (GC) and
marginal zone (MZ), broad MZ expansion with prominence of
immunophenotypically aberrant B cells (Ki B3-negative, CD5-positive),
possible predominance of paracortical plasma cells often with clusters of
clonal l-light chain restricted plasma cells, increase of paracortical
plasmacytoid monocytes, represent common hallmarks of CD. However, small
hyalinized and hypervascular GCs with hypervascular interfollicular stroma
and sinus effacement are common features of the HV variant, whereas
hyperplastic GCs with plasma cell aggregates in lymph node paracortex and
partially spared sinuses are characteristic features of the PC variant.
The frequent concomitance of the HV and PC types at separate sites,
together with transient morphological patterns from one type to the other
and from the localized to multicentric form during the course of the
disease, along with B and T cell impaired functions, with frequent
development of autoantibodies, have suggested that CD is a single disorder

related to immune dysregulation. A key event in the pathogenesis of CD has
been recently suggested to be an abnormal production of a B cell growth
factor, such as ***IL*** - ***6*** , leading to lymphoproliferation
and plasma cell differentiation and being involved in the oncogenesis of
plasmacytoma. In this event, Kaposi's sarcoma associated virus (***HHV*** - ***8***), which has been found in many cases of CD,
especially in the multicentric form, could play a crucial role both in
producing ***IL*** - ***6*** and releasing angiogenic factors. A
possible differentiation block may lead to the development of a malignant
lymphoma. Kaposi's sarcoma or other malignant neoplasias can be supposed
to be consequences of the immunodeficiency typical of CD.

L5 ANSWER 4 OF 16 MEDLINE
AN 2000053987 MEDLINE
DN 20053987
TI Human ***interleukin*** -6 is in vivo an autocrine growth factor for
human herpesvirus-8-infected malignant B lymphocytes.
AU Foussat A; Wijdenes J; Bouchet L; Gaidano G; Neipel F; Balabanian K;
Galanaud P; Couderc J; Emilie D
CS INSERM U. 131, Institut Paris-Sud sur les Cytokines, 32, rue des Carnets,
92140 Clamart, France.
SO EUROPEAN CYTOKINE NETWORK, (1999 Dec) 10 (4) 501-8.
Journal code: A56. ISSN: 1148-5493.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
EW 20000402
AB Human ***interleukin*** -6 (hIL-6) acts as a growth factor in several
human B lymphoid cancers. As human herpesvirus-8 (***HHV*** - ***8***) encodes for a viral ***IL*** - ***6*** (vIL-6), the viral cytokine
may be responsible for several manifestations of ***HHV*** - ***8*** -related disorders. Using an anti-hIL-6 mAb (B-E8) which does not
recognize vIL-6, we investigated the involvement of the human cytokine in
the proliferation of ***HHV*** - ***8*** -positive primary effusion
lymphoma (PEL) cells. In vitro, 5/5 PEL cell lines produced hIL-6 (4 to
1,200 pg/ml). The EBV- ***HHV*** - ***8*** + cell line (BCBL-1) was
adapted to grow in SCID mice. hIL-6 was detected in the serum of mice with
grafts, as well as human soluble CD138 (sCD138) and human IL-10 (hIL-10).
The serum level of these mediators increased with tumor progression. The
effect of treatment with the B-E8 mAb on the tumor progression and
survival was evaluated. This treatment significantly slowed down the tumor
development: on day 54, there were more mice with low levels of sCD138 and
hIL-10 in the treated group than in controls ($p = 0.03$ and 0.02,
respectively); treatment also delayed death (median date of death was day
65 for control mice and day 84 for anti-hIL-6 mAb-treated mice; $p < 0.02$).
Thus, hIL-6 is expressed in addition to vIL-6 in ***HHV*** - ***8*** -positive malignant B lymphocytes, and the viral cytokine does not totally
substitute for human ***IL*** - ***6*** in promoting tumor progression.

L5 ANSWER 5 OF 16 MEDLINE
AN 1999445405 MEDLINE
DN 99445405
TI Expression of cell-homologous genes of human herpesvirus-8 in human
immunodeficiency virus-negative lymphoproliferative diseases.
AU Luppi M; Barozzi P; Maiorana A; Trovato R; Marasca R; Morselli M; Cagossi
K; Torelli G
CS Department of Medical Sciences, Section of Hematology, Modena, Italy.
SO BLOOD, (1999 Oct 15) 94 (8) 2931-3.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 200001
EW 20000104
AB Human herpesvirus-8 (***HHV*** - ***8***) genome encodes for genes
homologous to human cellular genes such as ***interleukin*** -6 (
IL - ***6***), Cyclin-D, BCL-2, and IL-8 receptor (G-protein-coupled receptor [GCR]). We used reverse transcriptase-
polymerase chain reaction to study the expression of these viral genes in
lymphoproliferative disorders associated with ***HHV*** - ***8*** infection. None of these genes was expressed in 1 case of benign, localized Castleman's disease (CD), and only viral ***IL*** - ***6*** and viral Cyclin-D were transcribed in 2 cases of benign lymphadenopathies
with giant germinal center hyperplasia and increased vascularity. In
contrast, all 4 genes were transcribed in 1 case of multicentric CD of
plasma cell type with aggressive clinical course and in 1 primary effusion
lymphoma cell line. Our study provides the evidence that various ***HHV*** - ***8*** genes, homologous to cellular genes involved in
control of proliferation and apoptosis, may be differently expressed in
different lymphoid disorders in vivo.

L5 ANSWER 6 OF 16 MEDLINE
AN 1999441800 MEDLINE
DN 99441800
TI Human herpesvirus 8-encoded ***interleukin*** 6 activates HIV-1 in the
U1 monocytic cell line.
AU Gage J R; Breen E C; Echeverri A; Magpantay L; Kishimoto T; Miles S;
Martinez-Maza O
CS Department of Obstetrics and Gynecology, Osaka University, Japan.
NC CA57152 (NCI)
CA73475 (NCI)
F32CA80610 (NCI)
+
SO AIDS, (1999 Oct 1) 13 (14) 1851-5.
Journal code: AID. ISSN: 0269-9370.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200002
EW 20000204
AB OBJECTIVE: Human herpesvirus 8 (***HHV*** - ***8***) encodes a viral
interleukin 6 (vIL-6) which is structurally and functionally
similar to human ***interleukin*** 6 (hIL-6). Since hIL-6 has been
shown to upregulate the expression of HIV-1, the objectives of this study
were to examine the ability of vIL-6 to upregulate HIV-1, and to determine
the interactions of this virokine (viral cytokine) with the components of
the ***interleukin*** 6 (***IL*** - ***6***) receptor complex.
DESIGN AND METHODS: Recombinant ***HHV*** - ***8*** vIL-6 (rvIL-6)
was assayed for bioactivity in the ***IL*** - ***6*** -dependent cell

line MH60.BSF2. HIV-1 p24 production by the U1 monocytic and ACH-2 T-cell lines, which are chronically infected with HIV-1, was used to assess the ability of vIL-6 to affect HIV-1 expression. hIL-6 and vIL-6 receptor utilization was determined by quantifying HIV-1 p24 production after neutralization of components of the ***IL*** - ***6*** receptor complex, CD126'IL-6R' and CD130'gp130', on U1 cells with blocking antibodies. RESULTS: ***HHV*** - ***8*** rvIL-6 was seen to have ***IL*** - ***6*** -like bioactivity in MH60.BSF2 cells, and readily upregulated HIV-1 p24 production in U1 monocytic cells, but not in ACH-2 T cells. The vIL-6 appeared to utilize the ***IL*** - ***6*** -specific component of the ***IL*** - ***6*** signaling complex, CD126'IL-6R', in U1 cells. CONCLUSIONS: ***HHV*** - ***8*** vIL-6 clearly has the potential to upregulate HIV-1 expression in monocytic cells, and therefore may play a role in AIDS pathogenesis in individuals infected with both viruses.

L5 ANSWER 7 OF 16 MEDLINE
AN 1999412342 MEDLINE
DN 99412342
TI Human herpesvirus 8 ***interleukin*** -6 (vIL-6) signals through gp130 but has structural and receptor-binding properties distinct from those of human ***IL*** - ***6*** .
AU Wan X; Wang H; Nicholas J
CS Molecular Virology Laboratories, Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, Maryland 21231, USA.
NC R55 CA76445 (NCI)
RO1 CA76445 (NCI)
SO JOURNAL OF VIROLOGY, (1999 Oct) 73 (10) 8268-78.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199912
EW 19991203
AB Human herpesvirus 8 (***HHV*** - ***8***) has been associated with classical, endemic (African), and AIDS-related Kaposi's sarcoma (KS), body cavity-based primary effusion lymphomas, and multicentric Castleman's disease (MCD). ***HHV*** - ***8*** encodes a functional homologue of ***interleukin*** -6 (***IL*** - ***6***), a cytokine that promotes the growth of KS and myeloma cells and is found at elevated levels in MCD lesions and patient sera. We have previously reported that the viral ***IL*** - ***6*** (vIL-6) gene product can support the growth of the ***IL*** - ***6*** -dependent murine hybridoma cell line, B9, and that the gp80 (***IL*** - ***6*** receptor [IL-6R]) component of the ***IL*** - ***6*** receptor-signal transducer (gp180) complex plays a role in mediating this activity. However, it has been shown by others that vIL-6 can function in human cells independently of IL-6R. Here we have extended our functional studies of vIL-6 by identifying transcription factors and pathways used in human Hep3B cells, investigating the utilization of gp130 and IL-6R by vIL-6, and undertaking mutational analyses of vIL-6 and gp130. The data presented here establish that vIL-6, in common with its endogenous counterparts, can mediate signal transduction through gp130 and activate multiple transcription factors, map residues within the vIL-6 protein that are and are not important for vIL-6 signalling, and identify a gp130 mutant that is nonfunctional with respect to vIL-6 signalling in the absence of IL-6R but that retains the ability to mediate vIL-6 and human ***IL*** - ***6*** (hIL-6) signal transduction when IL-6R is coexpressed. The data presented demonstrate functional and mechanistic similarities between vIL-6 and endogenous ***IL*** - ***6*** proteins but also highlight differences in the structural and receptor-binding properties of vIL-6 relative to its human counterpart.

L5 ANSWER 8 OF 16 MEDLINE
AN 1999367590 MEDLINE
DN 99367590
TI Heterogeneity of viral ***IL*** - ***6*** expression in ***HHV*** - ***8*** -associated diseases.
AU Cannon J S; Nicholas J; Orenstein J M; Mann R B; Murray P G; Browning P J; DiGiuseppe J A; Cesarman E; Hayward G S; Ambinder R F
CS Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
NC UO1 CA70062 (NCI)
PO30 CA06973 (NCI)
PO30 CA68485 (NCI)
SO JOURNAL OF INFECTIOUS DISEASES, (1999 Sep) 180 (3) 824-8.
Journal code: IH3. ISSN: 0022-1899.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199911
EW 19991105
AB In order to characterize the expression of the viral ***interleukin*** -6 (vIL-6) homologue in various human herpesvirus 8 (***HHV*** - ***8***)-associated diseases, in situ hybridization and immunohistochemistry were applied to formalin-fixed specimens. These assays showed consistent expression of vIL-6 in primary effusion lymphomas and in a case of human immunodeficiency virus (HIV)-associated lymphadenopathy with a Castleman's disease-like appearance. In contrast, Kaposi's sarcoma specimens showed marked differences among specimens. In a consecutive series of specimens from the Johns Hopkins archives, vIL-6 expression was demonstrated in one of 13 cases. However, among 7 specimens selected from the AIDS Malignancy Bank because of their high levels of the T1.1 lytic transcript and virion production, vIL-6 expression was consistently demonstrated in infiltrating mononuclear cells and occasional spindle-shaped cells. Thus vIL-6 expression in clinical specimens correlates with other measures of the lytic viral cycle. Both assays generally give congruent results and are consistent with the possibility that vIL-6 expression plays a role in the pathogenesis of a variety of ***HHV*** - ***8*** -associated diseases.

L5 ANSWER 9 OF 16 MEDLINE
AN 1999292923 MEDLINE
DN 99292923
TI A rhesus macaque rhadinovirus related to Kaposi's sarcoma-associated herpesvirus/human herpesvirus 8 encodes a functional homologue of ***interleukin*** -6.
AU Kaleeba J A; Bergquam E P; Wong S W
CS Division of Pathobiology and Immunology, Oregon Regional Primate Research Center, Beaverton, Oregon 97006, USA.
NC CA75922 (NCI)

RR00163 (NCRR)
SO JOURNAL OF VIROLOGY, (1999 Jul) 73 (7) 6177-81.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199909
EW 19990905
AB The rhesus rhadinovirus strain 17577 (RRV strain 17577) genome is
essentially colinear with human herpesvirus 8 (HHV8)/Kaposi's sarcoma-associated herpesvirus (KSHV) and encodes several analogous open
reading frames (ORFs), including the homologue of cellular ***interleukin*** -6 (***IL*** - ***6***). To determine if the RRV
IL - ***6*** -like ORF (RvIL-6) is biologically functional, it
was expressed either transiently in COS-1 cells or purified from bacteria
as a glutathione S-transferase (GST)-RvIL-6 fusion and analyzed by
IL - ***6*** bioassays. Utilizing the ***IL*** - ***6***
-dependent B9 cell line, we found that both forms of RvIL-6 supported cell
proliferation in a dose-dependent manner. Moreover, antibodies specific to
the ***IL*** - ***6*** receptor (IL-6R) or the gp130 subunit were
capable of blocking the stimulatory effects of RvIL-6. Reciprocal
titrations of GST-RvIL-6 against human recombinant ***IL*** - ***6***
produced a more-than-additive stimulatory effect, suggesting that RvIL-6
does not inhibit but may instead potentiate normal cellular ***IL*** -
6 signaling to B cells. These results demonstrate that RRV encodes
an accessory protein with ***IL*** - ***6*** -like activity.

L5 ANSWER 10 OF 16 MEDLINE
AN 1999290757 MEDLINE
DN 99290757
TI Angiogenesis and hematopoiesis induced by Kaposi's sarcoma-associated
herpesvirus-encoded ***interleukin*** -6 [see comments].
CM Comment in: Blood 1999 Jun 15;93(12):4031-3
AU Aoki Y; Jaffe E S; Chang Y; Jones K; Teruya-Feldstein J; Moore P S; Tosato
G
CS Division of Hematologic Products, Center for Biologics Evaluation and
Research, Food and Drug Administration, Bethesda, MD, USA.. AOKI@CBER.FDA.GOV
SO BLOOD, (1999 Jun 15) 93 (12) 4034-43.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199909
EW 19990901
AB Kaposi's sarcoma-associated herpesvirus (KSHV; also known as human
herpesvirus 8 [***HHV*** - ***8***]) is a herpesvirus linked to the
development of Kaposi's sarcoma (KS), primary effusion lymphoma, and a
proportion of Castleman's disease. KSHV encodes viral ***interleukin***
-6 (vIL-6), which is structurally homologous to human and murine
IL - ***6*** . The biological activities of vIL-6 are largely
unknown. To gain insight into the biology of vIL-6, we expressed vIL-6 in
murine fibroblasts NIH3T3 cells and inoculated stable vIL-6-producing
clones into athymic mice. vIL-6 was detected selectively in the blood of
mice injected with vIL-6-expressing clones. Compared with controls,
vIL-6-positive mice displayed increased hematopoiesis in the myeloid,
erythroid, and megakaryocytic lineages; plasmacytosis in spleen and lymph
nodes; hepatosplenomegaly; and polyclonal hypergammaglobulinemia.
vIL-6-expressing NIH3T3 cells gave rise to tumors more rapidly than did
control cells, and vIL-6-positive tumors were more vascularized than
controls. Vascular endothelial growth factor (VEGF) was detected at higher
levels in the culture supernatant of vIL-6-expressing cells compared with
controls, and immunohistochemical staining detected VEGF in spleen, lymph
nodes, and tumor tissues from mice bearing vIL-6-producing tumors but not
control tumors. Thus, vIL-6 is a multifunctional cytokine that promotes
hematopoiesis, plasmacytosis, and angiogenesis. Through these functions,
vIL-6 may play an important role in the pathogenesis of certain KSHV-associated disorders.

L5 ANSWER 11 OF 16 MEDLINE
AN 1999229686 MEDLINE
DN 99229686
TI Constitutive cytokine production by primary effusion (body cavity-based)
lymphoma-derived cell lines.
AU Drexler H G; Meyer C; Gaidano G; Carbone A
CS DSMZ-German Collection of Microorganisms & Cell Cultures, Department of
Human and Animal Cell Cultures, Braunschweig.
SO LEUKEMIA, (1999 Apr) 13 (4) 634-40.
Journal code: LEU. ISSN: 0887-6924.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199907
EW 19990703
AB Primary effusion lymphoma (PEL) is a new lymphoma entity occurring
predominantly, but not exclusively in HIV+ patients with acquired
immunodeficiency syndrome (AIDS). PEL grows exclusively in body cavities
as serous lymphomatous effusion without evidence of mass disease or
dissemination. The cells are infected with the newly discovered human
herpesvirus-8 (***HHV*** - ***8***), often accompanied by co-infection with Epstein-Barr virus (EBV). Several lymphoma cell lines
have been established from patients with AIDS- and non-AIDS-associated
PEL. Given their phenotypical relationship to plasma cells, several
cytokines may be important for growth and survival of PEL cells. We
investigated the spectrum of cytokines produced by nine ***HHV*** -
8 + PEL cell lines, in comparison with five Burkitt lymphoma, seven
other B non-Hodgkin's lymphoma (B-NHL) and seven multiple myeloma-derived
cell lines. In addition, we tested the response of the PEL cells to
selected cytokines and the effects of neutralizing anti-cytokine and
anti-cytokine receptor antibodies. Using specific ELISAs, PEL cell lines
were found to produce large amounts of ***interleukin*** -6 (***IL***
- ***6*** ; 10-5000 pg/ml), ***IL*** - ***6*** soluble receptor
(IL-6sR; 30-600 pg/ml), IL-10 (600-80,000 pg/ml) and oncostatin M (OSM;
50-80 pg/ml) which in most cases were significantly higher than the levels
produced by the Burkitt, B-NHL or myeloma cell lines; on the contrary, PEL
cell lines did not elaborate significant levels of macrophage inhibitory
protein (MIP-1alpha) and leukemia inhibitory factor (LIF). However, the
levels of MIP-1alpha were increased 10- to 100-fold by treatment with
phorbol ester TPA. PEL cell lines did not respond proliferatively to

IL - ***6*** , IL-10, IL-11, LIF, MIP-1alpha, or OSM. Incubation
with IL-6sR and ***IL*** - ***6*** inhibited cell growth. Anti-IL6
neutralizing antibodies had no effect on PEL cell line proliferation; conversely, whereas anti-IL6R alone inhibited only weakly, anti-gp130 and
anti-gp130 plus anti-IL6R showed strong inhibitory effects (>20% inhibition in 5/9 lines and >60% inhibition in 3/9 lines). In summary, PEL
cell lines produce high amounts of cytokines (***IL*** - ***6*** ,
IL-10, OSM); proliferation could be inhibited by blocking the receptors of
the ***IL*** - ***6*** signaling pathway.

L5 ANSWER 12 OF 16 MEDLINE
AN 1998374965 MEDLINE
DN 98374965
TI Human herpesvirus type 8 and Kaposi's sarcoma.
AU Weiss R A; Whitby D; Talbot S; Kellam P; Boshoff C
CS Institute of Cancer Research, Chester Beatty Laboratories, London, U.K.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE. MONOGRAPHS, (1998) (23) 51-4.
Ref: 32
Journal code: ATR. ISSN: 1052-6773.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199811
EW 19981102
AB Kaposi's sarcoma-associated herpesvirus or human herpesvirus type 8 (
HHV - ***8***) is present in all forms of Kaposi's sarcoma (KS)
as well as in primary effusion lymphomas and some cases of Castleman's
disease. In KS tissues, ***HHV*** - ***8*** is present in endothelial and spindle cells. Current serologic tests suggest that
HHV - ***8*** is predominantly found in those at risk of KS and
is not as widespread as most other human herpesviruses. ***HHV*** -
8 encodes various proteins that may play a role in promotion of
cellular growth, including cyclin- and G-coupled protein receptor homologues, and anti-apoptotic proteins, including Bcl-2, ***IL*** -
6 (i.e., ***interleukin*** 6), and FLIP (i.e., FLICE inhibitory protein) homologues. In addition, ***HHV*** - ***8***
encodes two macrophage inflammatory-like proteins with anti-human
immunodeficiency virus and angiogenic potential.

L5 ANSWER 13 OF 16 MEDLINE
AN 1998158619 MEDLINE
DN 98158619
TI Human herpesvirus type 8 ***interleukin*** -6 homologue is functionally
active on human myeloma cells [see comments].
CM Comment in: Blood 1998 Sep 15;92(6):2186-8
AU Burger R; Neipel F; Fleckenstein B; Savino R; Ciliberto G; Kalden J R;
Gramatzki M
CS Division of Hematology/Oncology, Department of Medicine III, the Institute
for Clinical and Molecular Virology, University of Erlangen-Nuernberg,
Erlangen, Germany.
SO BLOOD, (1998 Mar 15) 91 (6) 1858-63.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199806
AB Seroepidemiology and polymerase chain reaction studies have strongly
suggested that human herpesvirus type 8 (***HHV*** - ***8***) is
associated with Kaposi's sarcoma, Castleman's disease, and body
cavity-based lymphoma. The genome of ***HHV*** - ***8*** harbors a
viral analogue of the ***interleukin*** -6 (***IL*** - ***6***)
gene. The amino acid sequence of the viral ***IL*** - ***6***
(vIL-6) protein is 24.7% identical to human ***IL*** - ***6***
(hIL-6). ***IL*** - ***6*** as a B-cell growth and differentiation
factor is known to play an essential role in the pathophysiology of B-cell
tumors. Thus, it seems possible that virus-encoded ***IL*** - ***6***
contributes to malignant growth of ***HHV*** - ***8*** -positive
B-cell lymphatic tumors. We have tested a preparation of ***HHV*** -
8 -derived ***IL*** - ***6*** for the ability to promote the
proliferation of the human myeloma cell line INA-6, which is strictly
dependent on exogenous ***IL*** - ***6*** for growth and survival.
Viral ***IL*** - ***6*** significantly induced DNA synthesis of
INA-6 cells, but required much more protein on a weight basis when
compared with hIL-6 for maximal proliferation. The proliferative effect of
vIL-6 was almost completely inhibited by a combination of anti-***IL***
- ***6*** receptor (IL-6R) and anti-gp130 antibodies or IL-6R superantagonist Sant7 and anti-gp130 antibodies. This report demonstrates
that vIL-6 has proliferative activity on human cells and that the IL-6R
and gp130 are involved in vIL-6 signaling in the myeloma cell line INA-6.

L5 ANSWER 14 OF 16 MEDLINE
AN 97208913 MEDLINE
DN 97208913
TI Kaposi's sarcoma-associated human herpesvirus-8 encodes homologues of
macrophage inflammatory protein-1 and ***interleukin*** -6.
AU Nicholas J; Ruvolo V R; Burns W H; Sandford G; Wan X; Ciufo D; Hendrickson
S B; Guo H G; Hayward G S; Reitz M S
CS Department of Oncology, Johns Hopkins University School of Medicine,
Baltimore, Maryland 21205, USA.
SO NATURE MEDICINE, (1997 Mar) 3 (3) 287-92.
Journal code: CG5. ISSN: 1078-8956.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U67774; GENBANK-U67775; GENBANK-U74585
EM 199706
AB Human herpesvirus-8 (***HHV*** - ***8***) has been detected in
Kaposi's sarcoma (KS) lesions of all types (AIDS-related, classical and
endemic), in body-cavity-based B-cell lymphomas (BCBLs) and in lesions of
multicentric Castleman's disease (MCD). We have identified a major
gamma-herpesvirus-divergent locus (DL-B) in ***HHV*** - ***8*** DNA
encoding several ***HHV*** - ***8*** unique open reading frames
(ORFs), including a homologue of ***interleukin*** -6 (***IL*** -
6) and two homologues of macrophage inflammatory protein MIP-1. We
show that the ***HHV*** - ***8*** -encoded ***IL*** - ***6***
homologue (vIL-6) shares functional properties with endogenous ***IL***
- ***6*** proteins and that both vIL-6 and vMIP-1 transcripts are
present at high levels following butyrate induction of an

HHV -
8 ' BCBL cell line. Low amounts of constitutive vIL-6, but not
vMIP-1, mRNA were also detected. The presence of a functional ***IL***
- ***6*** homologue encoded by ***HHV*** - ***8*** may provide a
mechanistic model for the hypothesized role of ***HHV*** - ***8***
in KS, MCD and BCBL that involves the mitogenic effects of vIL-6 on
surrounding cells. MIP-1 proteins may enhance these effects through the
chemotactic recruitment of endogenous cytokine-producing cells into
affected tissues and could potentially influence HIV disease progression
in coinfected individuals through interactions with the HIV co-receptor
CCR-5.

L5 ANSWER 15 OF 16 MEDLINE
AN 97138401 MEDLINE
DN 97138401
TI Human herpesvirus 8 encodes a homolog of ***interleukin*** -6.
AU Neipel F; Albrecht J C; Ensser A; Huang Y Q; Li J J; Friedman-Kien A E; Fleckenstein B
CS Institut fur Klinische und Molekulare Virologie, Universitat Erlangen-Nurnberg, Erlangen, Germany.. neipel@viro.med.uni-erlangen.de
SO JOURNAL OF VIROLOGY, (1997 Jan) 71 (1) 839-42.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U93872
EM 199704
AB Kaposi's sarcoma is a multifocal lesion that is reported to be greatly
influenced by cytokines such as ***interleukin*** -6 (***IL*** -
6) and oncostatin M. DNA sequences of a novel human
gammaherpesvirus, termed human herpesvirus 8 (***HHV*** - ***8***)
or Kaposi sarcoma-associated herpesvirus, have been identified in all
epidemiological forms of Kaposi's sarcoma with high frequency. The
presence of ***HHV*** - ***8*** DNA is also clearly associated with
certain B-cell lymphomas (body cavity-based lymphomas) and multicentric
Castleman's disease. Sequence analysis of a 17-kb fragment revealed that
adjacent to a block of conserved herpesvirus genes (major DNA-binding
protein, glycoprotein B, and DNA polymerase), the genome of ***HHV*** -
8 encodes structural homolog of ***IL*** - ***6*** . This
cytokine is involved not only in the pathogenesis of Kaposi's sarcoma but
also in certain B-cell lymphomas and multicentric Castleman's disease. The
viral counterpart of ***IL*** - ***6*** (vIL-6) has conserved
important features such as cysteine residues involved in disulfide
bridging or an amino-terminal signal peptide. Most notably, the region
known to be involved in receptor binding is highly conserved in vIL-6.
This conservation of essential features and the remarkable overlap between
diseases associated with ***HHV*** - ***8*** and diseases associated
with ***IL*** - ***6*** disregulation clearly suggest that vIL-6 is
involved in ***HHV*** - ***8*** pathogenesis.

L5 ANSWER 16 OF 16 MEDLINE
AN 97054369 MEDLINE
DN 97054369
TI The natural history and molecular heterogeneity of HIV-associated primary
malignant lymphomatous effusions.
AU Komanduri K V; Luce J A; McGrath M S; Herndier B G; Ng V L
CS Department of Medicine, University of California, San Francisco, USA.
NC RO1 CA54742 (NCI)
SO JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES AND HUMAN RETROVIROLOGY, (1996 Nov 1) 13 (3) 215-26.
Journal code: B7J. ISSN: 1077-9450.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
AB Primary malignant lymphomatous effusions arising in individuals infected
with the human immunodeficiency virus, type 1 (HIV-1) represent a rare
subset of HIV-associated lymphomas. Previous studies have demonstrated
that the malignant cells are monoclonal (as defined by rearrangement of
the immunoglobulin gene), express cell surface CD38, and are infected with
Epstein-Barr virus (EBV) and human herpes virus, type 8 (***HHV*** -
8). Despite these detailed molecular and immunophenotypic studies,
clinical information on this disease entity is scant, prompting us to
review the clinical features of eight cases seen at our institutions. All
eight patients had total peripheral CD4+ lymphocytes < 200/microliter and
presented with complaints related to body cavity distension. Routine
laboratory values were nondiagnostic and yielded no prognostic
information. Only two patients could tolerate and thus received
chemotherapy with no obvious impact on their clinical course. The mean
overall survival after diagnosis was 60 days (range 6-166 days). Four
patients were examined at autopsy. The primary malignant lymphomatous
effusion either was the immediate cause of death or contributed
significantly to the death of only two. All four patients examined post
mortem, however, had lymphomatous infiltration of serosal surfaces
adjacent to the site of the primary malignant effusion. Molecular and
immunologic studies performed on the malignant cells and effusion fluids
revealed universal expression of cell surface CD38 and the presence of
HHV - ***8*** gene sequences, but in contrast with previous
studies, only four had rearranged immunoglobulin genes or EBV present:
IL - ***6*** and IL-10 levels in the malignant effusion fluids
were markedly elevated. In summary, this rare subset of HIV-associated
lymphomas in our eight patients arose late in the course of HIV-associated
disease, had a rapid clinical course, and was molecularly heterogeneous. A
pathogenetic role for ***HHV*** - ***8*** alone in this disease
process is strengthened by our observation of four cases lacking EBV but
containing ***HHV*** - ***8*** .

=> s human herpesvirus type 8/ab,bi

7010318 HUMAN/BI
28829 HERPESVIRUS/BI
529956 TYPE/BI
749460 8/BI
5408175 AB/FA
43 HUMAN HERPESVIRUS TYPE 8/AB
((HUMAN(W)HERPESVIRUS(W)TYPE(W)8)/BI (L) AB/FA)
7010318 HUMAN/BI

28829 HERPESVIRUS/BI
529956 TYPE/BI
749460 8/BI
57 HUMAN HERPESVIRUS TYPE 8/BI
((HUMAN(W)HERPESVIRUS(W)TYPE(W)8)/BI)
L6 57 HUMAN HERPESVIRUS TYPE 8/AB,BI

=> s l6 and interleukin##/ab,bi

90769 INTERLEUKIN##/BI
5408175 AB/FA
59812 INTERLEUKIN##/AB
(INTERLEUKIN##/BI (L) AB/FA)
90769 INTERLEUKIN##/BI
L7 4 L6 AND INTERLEUKIN##/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 4 MEDLINE
AN 1999316867 MEDLINE
DN 99316867
TI The ***human*** ***herpesvirus*** - ***type*** ***8*** is
not involved in malignant melanoma.
AU Deichmann M; Thome M; Bock M; Jackel A; Waldmann V; Naher H
CS Universitats-Hautklinik Heidelberg, Germany.
SO BRITISH JOURNAL OF CANCER, (1999 Apr) 80 (1-2) 67-9.
Journal code: AV4. ISSN: 0007-0920.
CY SCOTLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199909
EW 19990902
AB Malignant melanomas were supposed to harbour the ***human***
herpesvirus - ***type*** ***8*** (HHV-8) genome, as melanoma
cells were reported to express ***interleukin*** -6 and a homologue of
interleukin -6 was found in the HHV-8 genome. We therefore
investigated 33 primary malignant melanomas by polymerase chain reaction,
but could not find this tumorigenic gamma-herpesvirus in any tumour.

L7 ANSWER 2 OF 4 MEDLINE
AN 1999223975 MEDLINE
DN 99223975
TI Involvement of human ***interleukin*** -6 in systemic manifestations of
human ***herpesvirus*** ***type*** ***8*** -associated
multicentric Castleman's disease [letter].
AU Foussat A; Fior R; Girard T; Boue F; Wijdenes J; Galanaud P; Emilie D
SO AIDS, (1999 Jan 14) 13 (1) 150-2.
Journal code: AID. ISSN: 0269-9370.
CY ENGLAND: United Kingdom
DT Letter
LA English
FS Priority Journals
EM 199909
EW 19990901

L7 ANSWER 3 OF 4 MEDLINE
AN 1998374965 MEDLINE
DN 98374965
TI ***Human*** ***herpesvirus*** ***type*** ***8*** and
Kaposi's sarcoma.
AU Weiss R A; Whitby D; Talbot S; Kellam P; Boshoff C
CS Institute of Cancer Research, Chester Beatty Laboratories, London, U.K.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE. MONOGRAPHS, (1998) (23) 51-4.
Ref: 32
Journal code: ATR. ISSN: 1052-6773.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199811
EW 19981102
AB Kaposi's sarcoma-associated herpesvirus or ***human*** ***herpesvirus*** ***type*** ***8*** (HHV-8) is present in all
forms of Kaposi's sarcoma (KS) as well as in primary effusion lymphomas
and some cases of Castleman's disease. In KS tissues, HHV-8 is present in
endothelial and spindle cells. Current serologic tests suggest that HHV-8
is predominantly found in those at risk of KS and is not as widespread as
most other human herpesviruses. HHV-8 encodes various proteins that may
play a role in promotion of cellular growth, including cyclin- and
G-coupled protein receptor homologues, and anti-apoptotic proteins,
including Bcl-2, IL-6 (i.e., ***interleukin*** 6), and FLIP (i.e.,
FLICE inhibitory protein) homologues. In addition, HHV-8 encodes two
macrophage inflammatory-like proteins with anti-human immunodeficiency
virus and angiogenic potential.

L7 ANSWER 4 OF 4 MEDLINE
AN 1998158619 MEDLINE
DN 98158619
TI ***Human*** ***herpesvirus*** ***type*** ***8***
interleukin -6 homologue is functionally active on human myeloma
cells [see comments].
CM Comment in: Blood 1998 Sep 15;92(6):2186-8
AU Burger R; Neipel F; Fleckenstein B; Savino R; Ciliberto G; Kalden J R;
Gramatzki M
CS Division of Hematology/Oncology, Department of Medicine III, the Institute
for Clinical and Molecular Virology, University of Erlangen-Nuernberg,
Erlangen, Germany.
SO BLOOD, (1998 Mar 15) 91 (6) 1858-63.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199806
AB Seroepidemiology and polymerase chain reaction studies have strongly
suggested that ***human*** ***herpesvirus*** ***type*** ***8*** (HHV-8) is associated with Kaposi's sarcoma, Castleman's
disease, and body cavity-based lymphoma. The genome of HHV-8 harbors a
viral analogue of the ***interleukin*** -6 (IL-6) gene. The amino acid
sequence of the viral IL-6 (vIL-6) protein is 24.7% identical to human
IL-6 (hIL-6). IL-6 as a B-cell growth and differentiation factor is known
to play an essential role in the pathophysiology of B-cell tumors. Thus,
it seems possible that virus-encoded IL-6 contributes to malignant growth
of HHV-8-positive B-cell lymphatic tumors. We have tested a preparation of
HHV-8-derived IL-6 for the ability to promote the proliferation of the
human myeloma cell line INA-6, which is strictly dependent on exogenous
IL-6 for growth and survival. Viral IL-6 significantly induced DNA
synthesis of INA-6 cells, but required much more protein on a weight basis
when compared with hIL-6 for maximal proliferation. The proliferative
effect of vIL-6 was almost completely inhibited by a combination of

anti-IL-6 receptor (IL-6R) and anti-gp130 antibodies or IL-6R superantagonist Sant7 and anti-gp130 antibodies. This report demonstrates
that vIL-6 has proliferative activity on human cells and that the IL-6R
and gp130 are involved in vIL-6 signaling in the myeloma cell line INA-6.

=> d his

(FILE 'HOME' ENTERED AT 16:30:20 ON 15 SEP 2000)

FILE 'MEDLINE' ENTERED AT 16:30:25 ON 15 SEP 2000
L1 14 S HERPES VIRUS TYPE 8/AB,BI
L2 1 S L1 AND INTERLEUKIN#/AB,BI
L3 458 S HHV-8/AB,BI
L4 38 S L3 AND INTERLEUKIN##/AB,BI
L5 16 S L4 AND IL-6/AB,BI
L6 57 S HUMAN HERPESVIRUS TYPE 8/AB,BI
L7 4 S L6 AND INTERLEUKIN##/AB,BI

=> file medline embase biosis inpadoc caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 5.74 5.89

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E3 235 --> FLECKENSTEIN BERNHARD/AU
E4 1 FLECKENSTEIN BERNHARD DR/AU
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E6 3 FLECKENSTEIN BERNHARD PROF/AU
E7 23 FLECKENSTEIN BERNHARD PROF DR/AU
E8 5 FLECKENSTEIN BERNHARD W/AU
E9 24 FLECKENSTEIN BURKHARD/AU
E10 8 FLECKENSTEIN BURKHARD T/AU
E11 10 FLECKENSTEIN CHRISTOPH/AU
E12 3 FLECKENSTEIN D/AU

=> s e1-e10

L8 312 ("FLECKENSTEIN BERNARD"/AU OR "FLECKENSTEIN BERNARD PROF"/AU OR "FLECKENSTEIN BERNHARD"/AU OR "FLECKENSTEIN BERNHARD DR"/AU OR "FLECKENSTEIN BERNHARD DR PROF"/AU OR "FLECKENSTEIN BERNHARD PROF"/AU OR "FLECKENSTEIN BERNHARD PROF DR"/AU OR "FLECKENSTEIN BERNHARD W"/AU OR "FLECKENSTEIN BURKHARD"/AU OR "FLECKENSTEIN BURKHARD T"/AU)

=> e albrecht jens-christian/au

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E6 1 ALBRECHT JIM/AU
E7 73 ALBRECHT JIRI/AU
E8 1 ALBRECHT JIRI DIPL ING/AU
E9 41 ALBRECHT JIRI ING CSC/AU
E10 55 ALBRECHT JOACHIM/AU
E11 23 ALBRECHT JOACHIM DR/AU
E12 2 ALBRECHT JOACHIM DR ING/AU

=> e albrecht jens christian/au

E1 18 ALBRECHT JENS/AU
E2 3 ALBRECHT JENS C/AU
E3 30 --> ALBRECHT JENS CHRISTIAN/AU
E4 2 ALBRECHT JENS DIPL ING/AU
E5 1 ALBRECHT JERRY L/AU
E6 6 ALBRECHT JERZY/AU
E7 1 ALBRECHT JIM/AU
E8 73 ALBRECHT JIRI/AU
E9 1 ALBRECHT JIRI DIPL ING/AU
E10 41 ALBRECHT JIRI ING CSC/AU
E11 55 ALBRECHT JOACHIM/AU
E12 23 ALBRECHT JOACHIM DR/AU

=> s e1-e3

L9 51 ("ALBRECHT JENS"/AU OR "ALBRECHT JENS C"/AU OR "ALBRECHT JENS CHRISTIAN"/AU)

=> e neipel frank/au

E1 1 NEIPALU V/AU
E2 82 NEIPEL F/AU
E3 62 --> NEIPEL FRANK/AU
E4 1 NEIPEL FRANK DR/AU
E5 1 NEIPEL M P/AU
E6 19 NEIPERT K V/AU
E7 4 NEIPERT M/AU
E8 2 NEIPERT M P/AU
E9 13 NEIPERT MARSHALL P/AU
E10 1 NEIPERT MARSHALL PALMER/AU
E11 1 NEIPLING J E/AU
E12 3 NEIPLING L/AU

=> s e2-e4

L10 145 ("NEIPEL F"/AU OR "NEIPEL FRANK"/AU OR "NEIPEL FRANK DR"/AU)

=> e friedman kien alvin/au

E1 79 FRIEDMAN KIEN A/AU
E2 338 FRIEDMAN KIEN A E/AU
E3 15 --> FRIEDMAN KIEN ALVIN/AU
E4 64 FRIEDMAN KIEN ALVIN E/AU
E5 1 FRIEDMAN KIEN U/AU
E6 1 FRIEDMAN KIENI A/AU
E7 6 FRIEDMAN KIM J/AU
E8 1 FRIEDMAN KLEIN A E/AU
E9 1 FRIEDMAN KLEN A/AU
E10 2 FRIEDMAN KURT E/AU
E11 933 FRIEDMAN L/AU
E12 82 FRIEDMAN L A/AU

=> s e1-e4

L11 496 ("FRIEDMAN KIEN A"/AU OR "FRIEDMAN KIEN A E"/AU OR "FRIEDMAN KIEN ALVIN"/AU OR "FRIEDMAN KIEN ALVIN E"/AU)

=> e huang yao qi/au

E1 2 HUANG YAO OI/AU
E2 3 HUANG YAO Q/AU
E3 42 --> HUANG YAO QI/AU
E4 1 HUANG YAO QUAN/AU
E5 2 HUANG YAO SHEN/AU
E6 4 HUANG YAO T/AU
E7 9 HUANG YAO TE/AU
E8 4 HUANG YAO TSENG/AU
E9 6 HUANG YAO TSUNG/AU
E10 4 HUANG YAO WEI/AU
E11 23 HUANG YAO WEN/AU
E12 6 HUANG YAO XIONG/AU

=> s e1-e4

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L12      48 ("HUANG YAO OI"/AU OR "HUANG YAO Q"/AU OR
"HUANG YAO QI"/AU OR
         "HUANG YAO QUAN"/AU)

=> d his


   (FILE 'HOME' ENTERED AT 16:30:20 ON 15 SEP 2000)

   FILE 'MEDLINE' ENTERED AT 16:30:25 ON 15 SEP 2000
L1       14 S HERPES VIRUS TYPE 8/AB,BI
L2        1 S L1 AND INTERLEUKIN#/AB,BI
L3      458 S HHV-8/AB,BI
L4       38 S L3 AND INTERLEUKIN##/AB,BI
L5       16 S L4 AND IL-6/AB,BI
L6       57 S HUMAN HERPESVIRUS TYPE 8/AB,BI
L7        4 S L6 AND INTERLEUKIN##/AB,BI

   FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS'
ENTERED AT 16:33:56 ON 15
   SEP 2000
         E FLECKENSTEIN BERNHARD/AU
L8       312 S E1-E10
         E ALBRECHT JENS-CHRISTIAN/AU
         E ALBRECHT JENS CHRISTIAN/AU
L9        51 S E1-E3
         E NEIPEL FRANK/AU
L10      145 S E2-E4
         E FRIEDMAN KIEN ALVIN/AU
L11      496 S E1-E4
         E HUANG YAO QI/AU
L12       48 S E1-E4

=> s l8 or l9 or l10 or l11 or l12

L13      937 L8 OR L9 OR L10 OR L11 OR L12

=> s l13 and (l1 or l3 or l6)

'AB' IS NOT A VALID FIELD CODE
L14       82 L13 AND (L1 OR L3 OR L6)

=> s l14 and interleukin?/ab,bi

'AB' IS NOT A VALID FIELD CODE
L15       20 L14 AND INTERLEUKIN?/AB,BI

=> dup rem l15

PROCESSING COMPLETED FOR L15
L16       10 DUP REM L15 (10 DUPLICATES REMOVED)

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 10 ANSWERS -
CONTINUE? Y/(N):y
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L16 ANSWER 1 OF 10 MEDLINE DUPLICATE 1
AN 2000053987 MEDLINE
DN 20053987
TI Human ***interleukin*** -6 is in vivo an autocrine growth factor for human herpesvirus-8-infected malignant B lymphocytes.
AU Foussat A; Wijdenes J; Bouchet L; Gaidano G; ***Neipel F*** ; Balabanian K; Galanaud P; Couderc J; Emilie D
CS INSERM U. 131, Institut Paris-Sud sur les Cytokines, 32, rue des Carnets, 92140 Clamart, France.
SO EUROPEAN CYTOKINE NETWORK, (1999 Dec) 10 (4) 501-8.
Journal code: A56. ISSN: 1148-5493.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
EW 20000402
AB Human ***interleukin*** -6 (hIL-6) acts as a growth factor in several human B lymphoid cancers. As human herpesvirus-8 (***HHV*** - ***g***) encodes for a viral IL-6 (vIL-6), the viral cytokine may be responsible for several manifestations of ***HHV*** - ***g*** -related disorders. Using an anti-hIL-6 mAb (B-E8) which does not recognize vIL-6, we investigated the involvement of the human cytokine in the proliferation of ***HHV*** - ***g*** -positive primary effusion lymphoma (PEL) cells. In vitro, 5/5 PEL cell lines produced hIL-6 (4 to 1,200 pg/ml). The EBV-***HHV*** - ***g*** + cell line (BCBL-1) was adapted to grow in SCID mice. hIL-6 was detected in the serum of mice with grafts, as well as human soluble CD138 (sCD138) and human IL-10 (hIL-10). The serum level of these mediators increased with tumor progression. The effect of treatment with the B-E8 mAb on the tumor progression and survival was evaluated. This treatment significantly slowed down the tumor development: on day 54, there were more mice with low levels of sCD138 and hIL-10 in the treated group than in controls ($p = 0.03$ and 0.02, respectively); treatment also delayed death (median date of death was day 65 for control mice and day 84 for anti-hIL-6 mAb-treated mice; $p < 0.02$). Thus, hIL-6 is expressed in addition to vIL-6 in ***HHV*** - ***g*** -positive malignant B lymphocytes, and the viral cytokine does not totally substitute for human IL-6 in promoting tumor progression.

L16 ANSWER 2 OF 10 MEDLINE
AN 1999276344 MEDLINE
DN 99276344
TI The role of ***HHV*** - ***g*** in Kaposi's sarcoma.
AU ***Neipel F*** ; Fleckenstein B
CS Institut fur Klinische und Molekulare Virologie, Universitat Erlangen-Numberg, Erlangen, D-91054, Germany.
SO SEMINARS IN CANCER BIOLOGY, (1999 Jun) 9 (3) 151-64. Ref: 82
Journal code: A6Y. ISSN: 1044-579X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199909
EW 19990901
AB The epidemiology of Kaposi's sarcoma (KS) amongst North American and Northern European patients with AIDS suggests that an infectious agent other than HIV is involved in its pathogenesis. Several lines of evidence indicate that human herpesvirus 8 (***HHV*** - ***g***), also termed Kaposi's sarcoma associated herpesvirus, is the sought after agent. DNA of ***HHV*** - ***g*** is invariably found in all forms of KS where the virus is present in the KS spindle cell. In contrast, ***HHV*** - ***g*** DNA is not regularly detected in most other malignancies. Antibodies against ***HHV*** - ***g*** are more frequently found in groups at risk of KS, and ***HHV*** - ***g*** seroconversion precedes KS development. Several ***HHV*** - ***g*** genes have been identified that exhibit transforming potential in cell culture systems. In addition, the virus encodes and induces several cytokines and angiogenic factors. This is of particular interest as models of KS pathogenesis developed before the discovery of ***HHV*** - ***g*** emphasized the importance of inflammatory cytokines. Although the expression pattern of viral genes in KS is not certain yet, it appears likely that the

pathogenetic role of ***HHV*** - ***8*** in KS may be rather complex
and differs from other virus-induced malignancies. 1999 Academic Press.

L16 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2000 ACS
AN 1998:89360 CAPLUS
DN 128:166368
TI The ***interleukin*** 6 of human herpesvirus 8 and its use in diagnostics and therapeutics
IN ***Fleckenstein, Bernhard*** ; ***Albrecht, Jens-Christian*** ; ***Neipel, Frank*** ; ***Friedman-Kien, Alvin*** ; ***Huang, *** *** Yao-Qi***
PA Behring Diagnostics G.m.b.H., Germany; New York University; Fleckenstein, Bernhard; Albrecht, Jens-Christian; Neipel, Frank; Friedman-Kien, Alvin; Huang, Yao-Qi
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9803657	A1	19980129	WO 1996-EP3199	19960719
W: US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 912742	A1	19990506	EP 1996-927558	19960719
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				

PRAI WO 1996-EP3199 19960719
AB Human herpesvirus 8 is found to carry a gene for an ***interleukin*** 6 that can bind to the ***interleukin*** 6 receptor. The ***interleukin*** and the gene encoding can be used in the diagnosis and treatment of a no. of diseases including: Kaposi sarcoma, Castleman's disease, multiple myeloma, kidney cell carcinoma, mesangial proliferative glomerulonephritis or B cell lymphoma. The protein may be manufd. by expression of the cloned gene.

L16 ANSWER 4 OF 10 MEDLINE DUPLICATE 2
AN 1998158619 MEDLINE
DN 98158619
TI ***Human*** ***herpesvirus*** ***type*** ***8*** ***interleukin*** -6 homologue is functionally active on human myeloma cells [see comments].
CM Comment in: Blood 1998 Sep 15;92(6):2186-8
AU Burger R; ***Neipel F*** ; Fleckenstein B; Savino R; Ciliberto G; Kalden J R; Gramatzki M
CS Division of Hematology/Oncology, Department of Medicine III, the Institute for Clinical and Molecular Virology, University of Erlangen-Nuernberg, Erlangen, Germany.
SO BLOOD, (1998 Mar 15) 91 (6) 1858-63.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199806
AB Seroepidemiology and polymerase chain reaction studies have strongly suggested that ***human*** ***herpesvirus*** ***type*** ***8*** (***HHV*** - ***8***) is associated with Kaposi's sarcoma, Castleman's disease, and body cavity-based lymphoma. The genome of ***HHV*** - ***8*** harbors a viral analogue of the ***interleukin*** -6 (IL-6) gene. The amino acid sequence of the viral IL-6 (vIL-6) protein is 24.7% identical to human IL-6 (hIL-6). IL-6 as a B-cell growth and differentiation factor is known to play an essential role in the pathophysiology of B-cell tumors. Thus, it seems possible that virus-encoded IL-6 contributes to malignant growth of ***HHV*** - ***8*** -positive B-cell lymphatic tumors. We have tested a preparation of ***HHV*** - ***8*** -derived IL-6 for the ability to promote the proliferation of the human myeloma cell line INA-6, which is strictly dependent on exogenous IL-6 for growth and survival. Viral IL-6 significantly induced DNA synthesis of INA-6 cells, but required much more protein on a weight basis when compared with hIL-6 for maximal proliferation. The proliferative effect of vIL-6 was almost completely inhibited by a combination of anti-IL-6 receptor (IL-6R) and anti-gp130 antibodies or IL-6R superantagonist Sant7 and anti-gp130 antibodies. This report demonstrates that vIL-6 has proliferative activity on human cells and that the IL-6R and gp130 are involved in vIL-6 signaling in the myeloma cell line INA-6.

L16 ANSWER 5 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:87733 BIOSIS
DN PREV199900087733
TI ***Human*** ***herpesvirus*** ***type*** ***8*** (***HHV*** - ***8***) IL-6 homologue induces proliferation of a human myeloma cell line: Involvement of the IL-6 receptor complex.
AU Burger, R.; ***Neipel, F.*** ; Savino, R.; Gramatzki, M.
CS Div. Hematol./Oncol., Dep. Med. III, Inst. Clin. Mol. Virol., Univ. Erlangen-Nuernberg, Erlangen Germany
SO Annals of Hematology, (1998) Vol. 77, No. SUPPL. 2, pp. S103. Meeting Info.: Annual Congress of the German and Austrian Societies of Hematology and Oncology Frankfurt, Germany October 25-28, 1998 Austrian Society of Hematology and Oncology . ISSN: 0939-5555.
DT Conference
LA English

L16 ANSWER 6 OF 10 MEDLINE DUPLICATE 3
AN 1998374969 MEDLINE
DN 98374969
TI Human herpesvirus 8--the first human Rhadinovirus.
AU ***Neipel F*** ; Albrecht J C; Fleckenstein B
CS Institut fur Klinische und Molekulare Virologie, Universitat Erlangen-Nurnberg, Germany.. fleckenstein@viro.med.uni-erlangen.de
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE. MONOGRAPHS, (1998) (23) 73-7.
Ref: 22
Journal code: ATR. ISSN: 1052-6773.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199811
EW 19981102
AB Kaposi's sarcoma (KS)-associated herpesvirus, also known as human herpesvirus 8 (***HHV*** - ***8***), is the first known human member of the genus Rhadinovirus. It is regularly found by polymerase chain reaction in all forms of KS, in certain types of Castleman's disease, and in body cavity-based B-cell lymphoma. Other members of this virus group occur in nonhuman primates, ungulates, rabbits, and mice and cause in part fulminant lymphomas and other neoplastic disorders of the

hematopoietic
system. Rhadinoviruses share a typical genome structure; most characteristically, they contain numerous sequences that appear to be
sequestered from cellular DNA. We cloned and sequenced almost the complete
genome of ***HHV*** - ***g*** from a single KS biopsy specimen.
Although this procedure revealed collinear organization and extensive
homologies with the open reading frames of herpesvirus saimiri, genes with
homology to the known oncoproteins (Stp, Tip) were not identified in the
HHV - ***g*** genome. However, ***HHV*** - ***g*** reading
frame K1, the positional analogue of Stp/Tip, was found to be
significantly variable between different strains. We found, in addition,
the reading frames for homologues of cellular ***interleukin*** 6,
macrophage inflammatory proteins alpha and beta (MIP1 alpha and MIP1 beta,
respectively), an interferon-responsive factor, and two inhibitors of
apoptosis. Several of these cell-homologous genes of ***HHV*** -
g have already been shown to code for functional proteins.

L16 ANSWER 7 OF 10 MEDLINE DUPLICATE 4
AN 97138401 MEDLINE
DN 97138401
TI Human herpesvirus 8 encodes a homolog of ***interleukin*** -6.
AU ***Neipel F*** ; Albrecht J C; Ensser A; Huang Y Q; Li J J; ***Friedman-Kien A E*** ; Fleckenstein B
CS Institut fur Klinische und Molekulare Virologie, Universitat Erlangen-Numberg, Erlangen, Germany..
neipel@viro.med.uni-erlangen.de
SO JOURNAL OF VIROLOGY, (1997 Jan) 71 (1) 839-42.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U93872
EM 199704
AB Kaposi's sarcoma is a multifocal lesion that is reported to be greatly
influenced by cytokines such as ***interleukin*** -6 (IL-6) and
oncostatin M. DNA sequences of a novel human gammaherpesvirus, termed
human herpesvirus 8 (***HHV*** - ***g***) or Kaposi
sarcoma-associated herpesvirus, have been identified in all
epidemiological forms of Kaposi's sarcoma with high frequency. The
presence of ***HHV*** - ***g*** DNA is also clearly associated with
certain B-cell lymphomas (body cavity-based lymphomas) and multicentric
Castleman's disease. Sequence analysis of a 17-kb fragment revealed that
adjacent to a block of conserved herpesvirus genes (major DNA-binding
protein, glycoprotein B, and DNA polymerase), the genome of ***HHV*** -
g encodes structural homolog of IL-6. This cytokine is involved
not only in the pathogenesis of Kaposi's sarcoma but also in certain
B-cell lymphomas and multicentric Castleman's disease. The viral
counterpart of IL-6 (vIL-6) has conserved important features such as
cysteine residues involved in disulfide bridging or an amino-terminal
signal peptide. Most notably, the region known to be involved in receptor
binding is highly conserved in vIL-6. This conservation of essential
features and the remarkable overlap between diseases associated with
HHV - ***g*** and diseases associated with IL-6 disregulation
clearly suggest that vIL-6 is involved in ***HHV*** - ***g***
pathogenesis.

L16 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:379203 BIOSIS
DN PREV199799678406
TI ***Human*** ***herpesvirus*** ***type*** ***g*** (
HHV - ***g***) ***interleukin*** -6 homolog is functionally
active on human plasma cells.
AU Burger, R. (1); ***Neipel, F.*** ; Fleckenstein, B.; Gramatzki, M.
CS (1) Div. Hematology/Oncol., Dep. Med. III, Univ. Erlangen-Nuernberg,
D-91054 Erlangen Germany
SO Journal of Molecular Medicine (Berlin), (1997) Vol. 75, No. 7, pp. B184.
Meeting Info.: XIX Symposium of the International Association for Comparative Research on Leukemia and Related Diseases Heidelberg, Germany
July 13-18, 1997
ISSN: 0946-2716.
DT Conference; Abstract
LA English

L16 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:66687 BIOSIS
DN PREV199800066687
TI ***Human*** ***herpesvirus*** ***type*** ***g*** (
HHV - ***g***) ***interleukin*** -6 homologue is functionally
active on human myeloma cells.
AU Gramatzki, M.; Burger, R.; ***Neipel, F.*** ; Fleckenstein, B.
CS Div. Hematology/Oncology, Dep. Med. III, Univ. Erlangen-Nuernberg, D-91054 Erlangen Germany
SO Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 1, pp. 87A.
Meeting Info.: 39th Annual Meeting of the American Society of Hematology
San Diego, California, USA December 5-9, 1997 The American Society of
Hematology
. ISSN: 0006-4971.
DT Conference
LA English

L16 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:327181 BIOSIS
DN PREV199799626384
TI Does ***HHV*** - ***g*** play a role in the pathogenesis of Kaposi's
sarcoma (KS): The study of the expression of vIL-6 and v-cyclin D in KS
tumor lesions.
AU ***Huang, Yao-Qi (1)*** ; Li, Jian-Jun (1); ***Neipel, Frank*** ;
Nicolaides, Alexander; ***Fleckenstein, Bernhard*** ;
Friedman-Kien, Alvin E. (1)
CS (1) Dep. Microbiol., NYU Med. Center, Erlangen Germany
SO Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology,
(1997) Vol. 14, No. 4, pp. A25.
Meeting Info.: National AIDS Malignancy Conference Bethesda, Maryland, USA
April 28-30, 1997
ISSN: 1077-9450.
DT Conference; Abstract
LA English

=> s (herpesvirus type 8 or human herpesvirus type 8 or herpes virus type 8 or hhv-8)/ab,bi

'AB' IS NOT A VALID FIELD CODE
L17 1800 (HERPESVIRUS TYPE 8 OR HUMAN HERPESVIRUS TYPE 8 OR HERPES VIRUS
TYPE 8 OR HHV-8)/AB,BI

=> s l17 and interleukin-6/ab,bi

'AB' IS NOT A VALID FIELD CODE
L18 124 L17 AND INTERLEUKIN-6/AB,BI

=> s l17 and (viral interleukin-6 or v-il-6)/ab,bi

'AB' IS NOT A VALID FIELD CODE
L19 29 L17 AND (VIRAL INTERLEUKIN-6 OR V-IL-6)/AB,BI

=> dup rem l19

PROCESSING COMPLETED FOR L19
L20 11 DUP REM L19 (18 DUPLICATES REMOVED)

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L20 ANSWER 1 OF 11 BIOSIS COPYRIGHT 2000 BIOSIS
AN 2000:324907 BIOSIS
DN PREV200000324907
TI Human herpesvirus 8-encoded interleukin-6 homologue (viral IL-6) induces
endogenous human IL-6 secretion.
AU Mori, Yasuko (1); Nishimoto, Norihiro; Ohno, Mika; Inagi, Reiko;
Dhepakson, Panadda; Amou, Kiyoko; Yoshizaki, Kazuyuki; Yamanishi, Koichi
CS (1) Department of Microbiology, Osaka University Medical School, Osaka
University, 2-2 Yamadaoka, Suita, Osaka, 565-0871 Japan
SO Journal of Medical Virology, (July, 2000) Vol. 61, No. 3, pp. 332-335.
print.
ISSN: 0146-6615.
DT Article
LA English
SL English
AB We found that human herpesvirus 8-encoded IL-6 (vIL-6) induced endogenous
human IL-6 (huIL-6) secretion from various cell lines (MT-4, THP-1, U937,
Raji, and CESS) including patients with multicentric Castleman's disease.
Especially, in MT-4 cells, huIL-6 was enhanced with vIL-6 by 30-fold
compared with that of control. In addition, reverse transcriptase-
polymerase chain reaction confirmed that vIL-6 induced huIL-6 expression
in MT-4 cells. Our novel finding of the huIL-6 induction by vIL-6
indicates that vIL-6 may play a significant role in the pathogenesis of
HHV - ***8*** associated diseases.

L20 ANSWER 2 OF 11 MEDLINE DUPLICATE 1
AN 1999214357 MEDLINE
DN 99214357
TI Cellular tropism and ***viral*** ***interleukin*** - ***6***
expression distinguish human herpesvirus 8 involvement in Kaposi's
sarcoma, primary effusion lymphoma, and multicentric Castleman's disease.
AU Staskus K A; Sun R; Miller G; Racz P; Jaslowski A; Metroka C; Brett-Smith
H; Haase A T
CS Department of Microbiology, University of Minnesota Medical School,
Minneapolis, Minnesota 55455, USA..
kathryn@lenti.med.umn.edu
NC CA-75172 (NCI)
CA-70036 (NCI)
SO JOURNAL OF VIROLOGY, (1999 May) 73 (5) 4181-7.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199907
EW 19990704
AB Human herpesvirus 8 (***HHV*** - ***8***) infection has been
implicated in the etiology of Kaposi's sarcoma (KS), primary effusion
lymphoma (PEL), and multicentric Castleman's disease (MCD), three diseases
that frequently develop in immunocompromised, human immunodeficiency
virus-positive individuals. One hypothesis that would account for
different pathological manifestations of infection by the same virus is
that viral genes are differentially expressed in heterogeneous cell types.
To test this hypothesis, we analyzed the localization and levels of
expression of two viral genes expressed in latent and lytic infections and
the viral homologue of interleukin-6 (vIL-6). We show that PEL parallels
KS in the pattern of latent and lytic cycle viral gene expression but that
the predominant infected cell type is a B cell. We also show that MCD
differs from KS not only in the infected cell type (B-cell and T-cell
lineage) but also in the pattern of viral gene expression. Only a few
cells in the lesion are infected and all of these cells express
lytic-cycle genes. Of possibly greater significance is the fact that in a
comparison of KS, PEL, and MCD, we found dramatic differences in the
levels of expression of vIL-6. Interleukin-6 is a B-cell growth and
differentiation factor whose altered expression has been linked to plasma
cell abnormalities, as well as myeloid and lymphoid malignancies. Our
findings support the hypothesis that ***HHV*** - ***8*** plays an
important role in the pathogenesis of PEL and MCD, in which vIL-6 acts as
an autocrine or paracrine factor in the lymphoproliferative processes
common to both.

L20 ANSWER 3 OF 11 MEDLINE DUPLICATE 2
AN 1999290757 MEDLINE
DN 99290757
TI Angiogenesis and hematopoiesis induced by Kaposi's sarcoma-associated
herpesvirus-encoded interleukin-6 [see comments].
CM Comment in: Blood 1999 Jun 15;93(12):4031-3
AU Aoki Y; Jaffe E S; Chang Y; Jones K; Teruya-Feldstein J; Moore P S; Tosato
G
CS Division of Hematologic Products, Center for Biologics Evaluation and
Research, Food and Drug Administration, Bethesda, MD, USA..
AOKI@CBER.FDA.GOV
SO BLOOD, (1999 Jun 15) 93 (12) 4034-43.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199909
EW 19990901
AB Kaposi's sarcoma-associated herpesvirus (KSHV; also known as human
herpesvirus 8 [***HHV*** - ***8***]) is a herpesvirus linked to the
development of Kaposi's sarcoma (KS), primary effusion lymphoma, and a
proportion of Castleman's disease. KSHV encodes ***viral*** ***interleukin*** - ***6*** (vIL-6), which is structurally homologous
to human and murine IL-6. The biological activities of vIL-6 are largely
unknown. To gain insight into the biology of vIL-6, we expressed vIL-6 in
murine fibroblasts NIH3T3 cells and inoculated stable vIL-6-producing
clones into athymic mice. vIL-6 was detected selectively in the blood of
mice injected with vIL-6-expressing clones. Compared with controls,
vIL-6-positive mice displayed increased hematopoiesis in the myeloid,
erythroid, and megakaryocytic lineages; plasmacytosis in spleen and lymph
nodes; hepatosplenomegaly; and polyclonal hypergammaglobulinemia.
vIL-6-expressing NIH3T3 cells gave rise to tumors more rapidly than did
control cells, and vIL-6-positive tumors were more vascularized

than
controls. Vascular endothelial growth factor (VEGF) was detected at higher
levels in the culture supernatant of vIL-6-expressing cells compared with
controls, and immunohistochemical staining detected VEGF in spleen, lymph
nodes, and tumor tissues from mice bearing vIL-6-producing tumors but not
control tumors. Thus, vIL-6 is a multifunctional cytokine that promotes
hematopoiesis, plasmacytosis, and angiogenesis. Through these functions,
vIL-6 may play an important role in the pathogenesis of certain
KSHV-associated disorders.

L20 ANSWER 4 OF 11 MEDLINE DUPLICATE 3
AN 1999441800 MEDLINE
DN 99441800
TI Human herpesvirus 8-encoded interleukin 6 activates HIV-1 in the U1
monocytic cell line.
AU Gage J R; Breen E C; Echeverri A; Magpantay L; Kishimoto T; Miles S;
Martinez-Maza O
CS Department of Obstetrics and Gynecology, Osaka University, Japan.
NC CA57152 (NCI)
CA73475 (NCI)
F32CA80610 (NCI)
+
SO AIDS, (1999 Oct 1) 13 (14) 1851-5.
Journal code: AID. ISSN: 0269-9370.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200002
EW 20000204
AB OBJECTIVE: Human herpesvirus 8 (***HHV*** - ***g***) encodes a
viral ***interleukin*** ***6*** (vIL-6) which is
structurally and functionally similar to human interleukin 6 (hIL-6).
Since hIL-6 has been shown to upregulate the expression of HIV-1, the
objectives of this study were to examine the ability of vIL-6 to
upregulate HIV-1, and to determine the interactions of this virokine
(viral cytokine) with the components of the interleukin 6 (IL-6) receptor
complex. DESIGN AND METHODS: Recombinant ***HHV*** - ***g*** vIL-6
(rvIL-6) was assayed for bioactivity in the IL-6-dependent cell line
MH60.BSF2. HIV-1 p24 production by the U1 monocytic and ACH-2 T-cell
lines, which are chronically infected with HIV-1, was used to assess the
ability of vIL-6 to affect HIV-1 expression. hIL-6 and vIL-6 receptor
utilization was determined by quantifying HIV-1 p24 production after
neutralization of components of the IL-6 receptor complex, CD126'IL-6R'
and CD130'gp130', on U1 cells with blocking antibodies. RESULTS:
HHV - ***g*** rvIL-6 was seen to have IL-6-like bioactivity in
MH60.BSF2 cells, and readily upregulated HIV-1 p24 production in U1
monocytic cells, but not in ACH-2 T cells. The vIL-6 appeared to utilize
the IL-6-specific component of the IL-6 signaling complex, CD126'IL-6R',
in U1 cells. CONCLUSIONS: ***HHV*** - ***g*** vIL-6 clearly has the
potential to upregulate HIV-1 expression in monocytic cells, and therefore
may play a role in AIDS pathogenesis in individuals infected with both
viruses.

L20 ANSWER 5 OF 11 MEDLINE DUPLICATE 4
AN 1999367590 MEDLINE
DN 99367590
TI Heterogeneity of viral IL-6 expression in ***HHV*** - ***g***
-associated diseases.
AU Cannon J S; Nicholas J; Orenstein J M; Mann R B; Murray P G; Browning P J;
DiGiuseppe J A; Cesarman E; Hayward G S; Ambinder R F
CS Department of Pharmacology, Johns Hopkins University School of Medicine,
Baltimore, Maryland, USA.
NC UO1 CA70062 (NCI)
PO30 CA06973 (NCI)
PO30 CA68485 (NCI)
SO JOURNAL OF INFECTIOUS DISEASES, (1999 Sep) 180 (3) 824-8.
Journal code: IH3. ISSN: 0022-1899.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199911
EW 19991105
AB In order to characterize the expression of the ***viral*** ***interleukin*** - ***6*** (vIL-6) homologue in various human
herpesvirus 8 (***HHV*** - ***g***)-associated diseases, in situ
hybridization and immunohistochemistry were applied to formalin-fixed
specimens. These assays showed consistent expression of vIL-6 in primary
effusion lymphomas and in a case of human immunodeficiency virus
(HIV)-associated lymphadenopathy with a Castleman's disease-like
appearance. In contrast, Kaposi's sarcoma specimens showed marked
differences among specimens. In a consecutive series of specimens from the
Johns Hopkins archives, vIL-6 expression was demonstrated in one of 13
cases. However, among 7 specimens selected from the AIDS Malignancy Bank
because of their high levels of the T1.1 lytic transcript and virion
production, vIL-6 expression was consistently demonstrated in infiltrating
mononuclear cells and occasional spindle-shaped cells. Thus vIL-6
expression in clinical specimens correlates with other measures of the
lytic viral cycle. Both assays generally give congruent results and are
consistent with the possibility that vIL-6 expression plays a role in the
pathogenesis of a variety of ***HHV*** - ***g*** -associated
diseases.

L20 ANSWER 6 OF 11 MEDLINE
AN 1999399397 MEDLINE
DN 99399397
TI Expression of human herpesvirus-8 (***HHV*** - ***g***) encoded
pathogenic genes in Kaposi's sarcoma (KS) primary lesions.
AU Ascherl G; Hohenadl C; Monini P; Zietz C; Browning P J; Ensoli B; Sturzl M
CS Max Planck Institute for Biochemistry, Department of Virology, Martinsried, Germany.
SO ADVANCES IN ENZYME REGULATION, (1999) 39 331-9.
Journal code: 2LG. ISSN: 0065-2571.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
EW 20000104
AB Transcription of six different ***HHV*** - ***g*** specific mRNAs
was examined in early- and late-stage KS primary lesions. Expression of
the latency-associated T0.7 mRNA and of VP23 mRNA which is a specific
marker of lytic/productive infection suggested that ***HHV*** - ***g*** is secondarily recruited into the KS lesions by productively
infected monocytes, macrophages. From these cells ***HHV*** - ***g***
is transmitted to the KS spindle cells, which are latently infected.
v-BCL-2, v-MCP-1 and ***v*** - ***IL*** - ***6*** were not

expressed in latently infected KS spindle cells, therefore the impact of these factors in KS pathogenesis appears to be low. By contrast, v-Cyclin D was highly expressed in almost all latently infected spindle cells and may therefore be an important factor triggering progression of late-stage KS lesions.

L20 ANSWER 7 OF 11 MEDLINE DUPLICATE 5
AN 1999131387 MEDLINE
DN 99131387
TI Induction of human herpesvirus-8 DNA replication and transcription by butyrate and TPA in BCBL-1 cells.
AU Yu Y; Black J B; Goldsmith C S; Browning P J; Bhalla K; Offermann M K
CS Winship Cancer Center, Emory University, Atlanta, GA 30322, USA.
NC RO1 CA67382 (NCI)
P30AR42687 (NIAMS)
SO JOURNAL OF GENERAL VIROLOGY, (1999 Jan) 80 (Pt 1) 83-90.
Journal code: I9B. ISSN: 0022-1317.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199905
EW 19990502
AB Human herpesvirus-8 (***HHV*** - ***8***) is a gammaherpesvirus that is present primarily in a state of low level persistence in primary effusion lymphoma cell lines. Using BCBL-1 cells that harbour ***HHV*** - ***8*** but lack Epstein-Barr virus, we demonstrate that sodium butyrate is much more effective than the phorbol ester 12-O-tetradecanoyl phorbol-13-acetate (TPA) at inducing high levels of class II and III virus transcription and viral DNA replication, but also initiates apoptosis. Apoptosis occurs prior to assembly of virions when high concentrations of butyrate (1-3 mM) are used, whereas reduction of butyrate concentration to 0.3 mM decreases the rate of apoptosis and results in production and secretion of enveloped virions that are visualized at high number by electron microscopy in approximately 20% of BCBL-1 cells. Butyrate induces much higher levels of multiple class II and class III transcripts than does TPA, including v-MIP1, ***v*** - ***IL*** - ***6*** , v-Bcl-2, vGPCR and ORF26. A decrease in concentration of butyrate from 3 to 0.3 mM delays the peak induction of these genes, but peak levels remain higher than peak levels in response to TPA. These studies indicate that the massive apoptosis induced by 3 mM butyrate could be diminished and delayed by reduction of butyrate concentration to 0.3 mM, thereby allowing expression of high levels of lytic-associated genes and production of high yields of ***HHV*** - ***8*** virions.

L20 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:379732 BIOSIS
DN PREV199900379732
TI KSHV/ ***HHV*** - ***8*** interleukin-6 (vIL6) expression in HIV-related lymphadenopathy correlates with development of Kaposi's sarcoma and survival.
AU Chadburn, A. (1); Hyjek, E. (1); Ying, L. (1); Mulligan, L. (1); Knowles, D. M. (1); Cesarman, E. (1)
CS (1) Weill Medical College-Cornell University, New York, NY USA
SO JAIDS Journal of Acquired Immune Deficiency Syndromes, (May 1, 1999) Vol. 21, No. 1, pp. A21.
Meeting Info.: Third National AIDS Malignancy Conference Bethesda, Maryland, USA May 26-27, 1999
DT Conference
LA English

L20 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2000 ACS
AN 1998:89360 CAPLUS
DN 128:166368
TI The interleukin 6 of human herpesvirus 8 and its use in diagnostics and therapeutics
IN Fleckenstein, Bernhard; Albrecht, Jens-Christian; Neipel, Frank; Friedman-Kien, Alvin; Huang, Yao-Qi
PA Behring Diagnostics G.m.b.H., Germany; New York University; Fleckenstein, Bernhard; Albrecht, Jens-Christian; Neipel, Frank; Friedman-Kien, Alvin; Huang, Yao-Qi
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9803657	A1	19980129	WO 1996-EP3199	19960719
W: US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 912742	A1	19990506	EP 1996-927558	19960719
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
PRAI WO 1996-EP3199		19960719		

AB Human herpesvirus 8 is found to carry a gene for an interleukin 6 that can bind to the interleukin 6 receptor. The interleukin and the gene encoding can be used in the diagnosis and treatment of a no. of diseases including: Kaposi sarcoma, Castleman's disease, multiple myeloma, kidney cell carcinoma, mesangial proliferative glomerulonephritis or B cell lymphoma. The protein may be manufd. by expression of the cloned gene.

L20 ANSWER 10 OF 11 MEDLINE DUPLICATE 6
AN 97184526 MEDLINE
DN 97184526
TI A single 13-kilobase divergent locus in the Kaposi sarcoma-associated herpesvirus (human herpesvirus 8) genome contains nine open reading frames that are homologous to or related to cellular proteins.
AU Nicholas J; Ruvolo V; Zong J; Ciufo D; Guo H G; Reitz M S; Hayward G S
CS Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, Maryland 21231, USA.
NC U01 CA37314 (NCI)
R01 CA73585 (NCI)
P30 CA06973 (NCI)
SO JOURNAL OF VIROLOGY, (1997 Mar) 71 (3) 1963-74.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U67774; GENBANK-U67775; GENBANK-U74585; GENBANK-U83347; GENBANK-U83348; GENBANK-U83349; GENBANK-U83350; GENBANK-U83351; GENBANK-U85269
EM 199705
AB Two small fragments of a novel human gammaherpesvirus genome known as Kaposi's sarcoma (KS)-associated herpesvirus or human herpesvirus 8 (***HHV*** - ***8***) have been shown to be present in virtually all AIDS and non-AIDS KS lesions, as well as in body cavity-based lymphomas (BCBL) and in multicentric Castleman's disease. We have extended those studies by identifying and sequencing a third fragment of

HHV -
g DNA encoding a viral thymidylate synthetase (TS) gene. Use of
this viral TS fragment as a probe led to the identification and mapping of
a cluster of overlapping phage lambda clones from a BCBL tumor DNA genomic
library that spanned 48 kb on the left-hand side of the ***HHV*** -
g genome between the equivalents of open reading frame 6 (ORF6)
and ORF31 of herpesvirus saimiri (HVS). DNA sequencing of a 17-kb segment
encompassing a gammaherpesvirus divergent locus (DL-B) between ORF11 and
ORF17 revealed the presence of nine viral ORFs with predicted gene
products related to cellular proteins. These include the complete TS gene
and a dihydrofolate reductase (DHFR) gene, four novel cytokine genes
(encoding ***viral*** ***interleukin*** - ***6*** , viral MIP-1A,
viral MIP-1B, and BCK) that have not previously been found to be encoded
by a virus, and a bcl-2 homolog. This region in ***HHV*** - ***g***
also contains the T1.1 abundant lytic cycle nuclear RNA gene and
encompasses two genes (or exons) encoding proteins with C4HC3 zinc finger
domains of the PHD/leukemia-associated protein subtype. The latter are
related to the spliced immediate-early IE1 protein of the gamma-2 class
herpesvirus bovine herpesvirus type 4 and a similar motif found in HVS
ORF12. Although genes for TS and DHFR enzymes are also encoded by HVS
(ORF70 and ORF2), both occur at different genomic loci than in ***HHV***
- ***g*** , and the ***HHV*** - ***g*** DHFR protein is much
farther diverged from human DHFR than is the HVS version, implying that
they were probably acquired as host cell cDNAs by independent evolutionary
events. Transcripts from the IE1-A, IE1-B, DHFR, and MIP-1B genes were all
detected by Northern blot hybridization analysis in a BCBL cell line at 12
h after induction with butyrate but were not present before induction,
indicating that these are all primarily lytic cycle genes. We conclude
that the DL-B locus of gammaherpesviruses displays considerably more
variability that previously appreciated and that expression of many of
these genes is likely to have important implications for ***HHV*** -
g biology and therapy.

L20 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:327181 BIOSIS
DN PREV199799626384
TI Does ***HHV*** - ***g*** play a role in the pathogenesis of Kaposi's
sarcoma (KS): The study of the expression of vIL-6 and v-cyclin D in KS
tumor lesions.
AU Huang, Yao-Qi (1); Li, Jian-Jun (1); Neipel, Frank; Nicolaides, Alexander;
Fleckenstein, Bernhard; Friedman-Kien, Alvin E. (1)
CS (1) Dep. Microbiol., NYU Med. Center, Erlangen Germany
SO Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology,
(1997) Vol. 14, No. 4, pp. A25.
Meeting Info.: National AIDS Malignancy Conference Bethesda, Maryland, USA
April 28-30, 1997
ISSN: 1077-9450.
DT Conference; Abstract
LA English

=> d his

(FILE 'HOME' ENTERED AT 16:30:20 ON 15 SEP 2000)

FILE 'MEDLINE' ENTERED AT 16:30:25 ON 15 SEP 2000
L1 14 S HERPES VIRUS TYPE 8/AB,BI
L2 1 S L1 AND INTERLEUKIN#/AB,BI
L3 458 S HHV-8/AB,BI
L4 38 S L3 AND INTERLEUKIN##/AB,BI
L5 16 S L4 AND IL-6/AB,BI
L6 57 S HUMAN HERPESVIRUS TYPE 8/AB,BI
L7 4 S L6 AND INTERLEUKIN##/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 16:33:56 ON 15
SEP 2000
E FLECKENSTEIN BERNHARD/AU
L8 312 S E1-E10
E ALBRECHT JENS-CHRISTIAN/AU
E ALBRECHT JENS CHRISTIAN/AU
L9 51 S E1-E3
E NEIPEL FRANK/AU
L10 145 S E2-E4
E FRIEDMAN KIEN ALVIN/AU
L11 496 S E1-E4
E HUANG YAO QI/AU
L12 48 S E1-E4
L13 937 S L8 OR L9 OR L10 OR L11 OR L12
L14 82 S L13 AND (L1 OR L3 OR L6)
L15 20 S L14 AND INTERLEUKIN?/AB,BI
L16 10 DUP REM L15 (10 DUPLICATES REMOVED)
L17 1800 S (HERPESVIRUS TYPE 8 OR HUMAN HERPESVIRUS TYPE 8 OR HERPES VIR
L18 124 S L17 AND INTERLEUKIN-6/AB,BI
L19 29 S L17 AND (VIRAL INTERLEUKIN-6 OR V-IL-6)/AB,BI
L20 11 DUP REM L19 (18 DUPLICATES REMOVED)

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FULL ESTIMATED COST		153.92	159.81

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

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UI 9720891 3

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UI 20053987

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UI 99445405

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